NOVEL ROUTES TO INSECT SEX-PHEROMONES AND MACROLIDES *VIA* ACETYLENIC SYNTHONS FROM CASTOR OIL

A Thesis Submitted
in Partial Fulfilment of the Requirements
for the Degree of

DOCTOR OF PHILOSOPHY

by

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to the

DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY KANPUR

JUNE, 1982

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India, under the supervision of Professor S. Ranganathan.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

Vibha Maniktala

Vibha Maniktala

CERTIFICATE

Certified that the work contained in this thesis, entitled, 'NOVEL ROUTES TO INSECT SEX-PHEROMONES AND MACROLIDES VIA ACETYLENIC SYNTHONS FROM CASTOR OIL' has been carried out by Vibha Maniktala under my supervision and the same has not been submitted elsewhere for a degree.

(S. Ranganathan)
Thesis Supervisor

Kanpur
June 1982

DEPARTMENT OF CHEMISTRY
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CERTIFICATE OF COURSE WORK

This is to certify that Miss Vibha Maniktala has satisfactorily completed all the course requirements for the Ph.D. degree programme. The courses include:

Chm 501	Advanced Organic Chemistry I
Chm 502	Advanced Organic Chemistry II
Chm 521	Chemical Binding
Chm 524	Modern Physical Methods in Chemistry
Chm 541	Advanced Inorganic Chemistry I

Credits related to Chm 521 and Chm 524 were transferred from

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No sense of caution governs my gratitude towards those who helped with this thesis. First and foremost, I wish to thank Professor S. Ranganathan for his encouragement, advice and continuous guidance which, in a way, revived my interest in the subject. I am grateful to him for his detailed comments on the contents of this manuscript and for the uncounted hours spent in bringing it to its present form.

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I would also like to thank, Dr. David R. Hall, Tropical Products' Institute, London for his painstaking interest and expert help in providing the GC traces; Dr. S.P. Popli, Head, Medicinal Chemistry Division, C.D.R.I., Lucknow and Dr. R.S.Kapil for providing spectroscopic facilities; Dr. Ramachandran, Director, DRL, Gwalior, Dr. R. Vaidyanathaswamy, Dr. Lakshmana Rao and Mr. K. Sampath for allowing us access to nmr facilities; Dr. T.R. Govindachari, Research and Development Department,

Amrutanjan, Madras, for spectroscopic facilities and Professor J. Fried, Chicago, for providing the 500 MHz spectrum.

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Vibha Maniktala

PREFACE

NOVEL ROUTES TO INSECT SEX-PHEROMONES AND MACROLIDES VIA ACETYLENIC SYNTHONS FROM CASTOR OIL

Castor oil, 12-hydroxy octadec (Z) 9-enoic acid glycerol triester, is an abundantly available natural product. It is almost a single compound ($\sim$93% ricinoleic ester) and the unique γ, δ-unsaturated moiety present imparts to it an exceptionally high versatility. Methanolysis of castor oil gives, readily, methyl 12-hydroxy octadec (Z) 9-enoate (1*). Thermally, 1 fragments by a $\pi^2s + \sigma^2s + \sigma^2s$ process to methyl undec 10-enoate (2) and heptaldehyde (3). With hot aqueous alkali, 1 undergoes a deep-seated re-arrangement leading to decane 1,10 dioic acid (sebacic acid, 53), 2-octanol and 2-octanone.

In the present work, as an appropriate illustration of the current, appealing, facet of the art in organic synthesis, namely, the metamorphosis of readily available natural products to structures of current interest and utility, compounds 2, 3 and 53 have been converted to, via novel synthons and strategies, invariably in good yields and high stereochemical purity - on the basis of GC analysis of representative samples on a liquid crystal

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* These numbers refer to those presented in the thesis, Section C.

column - a number of insect sex pheromones that are of current attraction. Additionally, practical routes to vaccenic acid (36), the macrolide, recifeiolide (70) and traumatin (86) have been delineated.

The C-18 castor oil bears a striking resemblance to the C-18 insect sex pheromones of Achroia grisella, 1-oxo octadec (Z) 11-ene (17) and Lycorea ceres ceres, 1-acetoxy octadec (Z) 11-ene (19). In the present work, 1 has been re-structured to 17 and 19 via key acetylide coupling of the novel synthon 1-tetrahydropyranyloxy dodec 11-yne (8) with n-hexyl bromide (13). The homologation of 2 to the key synthon 8 was accomplished by sequence, LAH reduction and DHP protection to 1-tetrahydropyranyloxy undec 10-ene (5), hydroboration-PCC oxidation to 1-tetrahydropyranyloxy undecanal (6), Wittig reaction with $Ph_3P{=}CBr_2$ to 1-tetrahydropyranyloxy 12,12 dibromo dodec 11-ene (7) and dehalogenation with Li-Hg. The degradation of 3 to 13 was achieved by transformation to 1-acetoxy 1-heptene (9), CrO_3-Ac_2O oxidation to hexanoic acid (10), esterification, LAH reduction and PBr_3 treatment. Alkylation of acetylide generated from 8 by n-BuLi-HMPT with n-hexyl bromide gave, 1-tetrahydropyranyloxy octadec 11-yne (14). Deprotection of 14 with PPTS-EtOH gave 1-hydroxy octadec 11-yne which on stereoselective hydrogenation and PCC oxidation gave 1-oxo octadec (Z) 11-ene (17), the sex pheromone of Achroia grisella. Direct-OTHP→ -OAc transformation of 14 with AcOH:AcCl

followed by stereoselective hydrogenation gave 1-acetoxy octadec (Z) 11-ene (19), the sex pheromone of Lycorea ceres ceres. GC analysis on a liquid crystal column showed that the stereochemical purity of 19 is 98.3% of the Z isomer.

1-Tetrahydropyranyloxy dodec 11-yne (8) has been demonstrated to be a good synthon for insect sex pheromones of the type $R-CH=CH-(CH_2)_9-CH_2X$.

Alkylation of the conjugate base of 8 with n-BuBr gave 1-tetrahydropyranyloxy hexadec 11-yne (20) and with EtBr, 1-tetrahydropyranyloxy tetradec 11-yne (25). De-protection of 20 and 25 followed by stereoselective hydrogenation gave, 1-hydroxy hexadec (Z) 11-ene (22) and 1-hydroxy tetradec (Z) 11-ene (27), the sex pheromones related to, respectively, Mamestra configurata and Archips rosanus. Direct -OTHP $\longrightarrow$ -OAc transformation of 20 and 25, followed by stereoselective hydrogenation gave 1-acetoxy hexadec (Z) 11-ene (24) and 1-acetoxy tetradec (Z) 11-ene (29), the sex pheromones related to, respectively, Scotogramma trifolii and Choristoneura rosaceana. GC analysis of 29 on a special liquid crystal column demonstrated that it contained, at least, 95% of the desired Z-isomer. A similar selectivity for 24 has been deduced from such an analysis on its lower homolog.

Reduction of 25 with sodium-liquid ammonia gave, 1-tetrahydropyranyloxy tetradec (E) 11-ene (30) which, on de-protection, gave 1-hydroxy tetradec (E) 11-ene (31), the sex pheromone of

Archips argyrospylus, and on direct -OTHP ⟶ -OAc change led to 1-acetoxy tetradec (E) 11-ene (32), the sex pheromone of Platyonota stultana.

A practical route to the rare fatty acid, octadec (Z) 11-enoic acid (36, vaccenic acid) has been achieved from the key synthon 8 by sequence, de-protection, Jones' oxidation, alkylation and stereoselective hydrogenation.

The versatility of sebacic acid (53), the degradation product of castor oil with hot alkali, as a useful synthon has been illustrated by its transformation to non 8-ynoic acid (57), which, in turn, has been demonstrated to be a good precursor for insect sex pheromones and macrolides.

The 53 ⟶ 57 change incorporates a surprisingly, extraordinarily regioselective, decarboxylative π generation. Thus, decane 1,10-dioic acid monomethyl ester (55), prepared by preferential saponification of the di-ester with $Ba(OH)_2.8H_2O$, gave, cleanly, on treatment with $Pb(OAc)_4$-$Cu(OAc)_2$, methyl non 8-enoate (56) with no detectable (NMR) amounts of the internal olefin. The latter was transformed to non 8-ynoic acid (57) by addition of Br_2 followed by careful dehydrohalogenation.

No clean procedure is presently available for the terminal π ⟶ lower terminal π change. In the present work, such a change has been illustrated with the methyl undec 10-enoate (2) ⟶ methyl dec 9-enoate (49) transformation via

methyl undecane 1,11 dioic acid monoester (73), which was prepared from 2 by hydroboration and CrO_3-H_2SO_4 treatment. Parenthetically, 49 is a key prostaglandin synthon.

1-Tetrahydropyranyloxy non 8-yne (62), readily prepared from non 8-ynoic acid (57) via esterification to methyl non 8-ynoate (60), LAH reduction and DHP protection, could be anticipated to be a useful synthon for the preparation of insect sex pheromones of the type R-CH=CH-$(CH_2)_6$-CH_2X. This has been demonstrated with the synthesis of, from 62, 1-acetoxy dodec (Z) 8-ene (65), the sex pheromone related to Grapholita molesta by sequence, n-PrBr alkylation, direct -OTHP ⟶ -OAc change and stereoselective hydrogenation.

The naturally occurring macrolide, recifeiolide (70), has been reached, in the present work, by an exceptionally short route from sebacic acid (53) via the key synthon non 8-ynoic acid (57) by selective acetylide alkylation with 1-bromo 2-hydroxy propane (67), followed by sodium-liquid ammonia reduction and cyclization. The alkylation step, however, needs to be improved greatly.

Bombykol, a very important insect sex pheromone related to Bombyx mori - a common form of silkworm moth - has been synthesized, in good overall yields and excellent stereochemical purity, from methyl undec 10-enoate (2), the thermal fragmentation product from castor oil.

1-Tetrahydropyranyloxy undec 10-yne (78) - readily derived from 2 by Br_2 addition, alkali mediated dehydrohalogenation and esterification to methyl undec 10-enoate (76) followed by LAH reduction and DHP protection - on hydroxymethylation with n-BuLi-$(CH_2O)_n$, hydrogenation and PCC oxidation gave 1-tetrahydropyranyloxy 12-oxo dodec (E) 10-ene (81), which, on carefully controlled Wittig reaction with $Ph_3P{=}CHC_3H_7$ followed by deprotection, gave 1-hydroxy hexadeca 10(E), 12(Z)-diene (83), bombykol. GC analysis on a liquid crystal column showed that 83 contained 89.3% of the desired E, Z isomer. Hydroxymethylation of 76 with Cu_2O-formalin followed by hydrogenation and PCC oxidation gave methyl 12-oxo dodec (E) 10-enoate (86), the methyl ester of the naturally occurring rare aldehyde acid, traumatin.

CONTENTS

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A. INTRODUCTION

The present work endeavours to illustrate an attractive and useful facet of the art in organic synthesis, namely, the metamorphosis of readily available natural products to structures of current interest and utility.

Long chain, saturated and unsaturated, fatty acids bear a striking structural similarity to a variety of rare natural products of current interest, such as, insect sex pheromones, prostaglandins and macrolides and, therefore, the tools available for organic synthesis can, in principle, be used to re-structure fatty acids to a variety of other natural products.

Amongst the fatty acids that are abundantly available in nature, castor oil offers the maximum advantage. Unlike most other naturally occurring oils it is almost a single compound ($\sim$ 93% ricinoleic ester) and is singularly gifted with functional groups that could be operated upon, either individually or in concert. Particularly, the unique γ, δ-unsaturated moiety present in castor oil imparts to it an exceptionally high

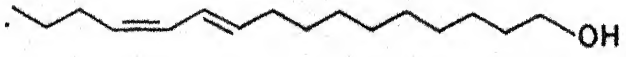
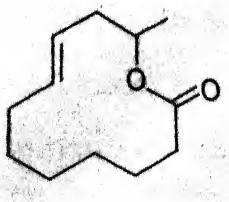
versatility. Thus, thermally, methyl ricinoleate fragments by a $\pi^2s + \sigma^2s + \sigma^2s$ process to methyl undec 10-enoate and heptaldehyde, and with hot aqueous alkali it undergoes a practical, deep-seated rearrangement leading to decane 1,10-dioic acid (sebacic acid).

In the present work, methyl undec 10-enoate and decane 1,10-dioic acid have been transformed *via* novel synthons and strategies, invariably in good yields and with high stereochemical purity - on the basis of GC analysis of representative samples on a liquid crystal column - to a number of insect sex pheromones that are of current attraction. Additionally, practical routes to vaccenic acid, traumatin and the naturally occurring macrolide, recifeiolide, have been delineated (Chart A.I).

As a broad base for the present work, it was considered appropriate to provide a background that has, as the focus, organic synthesis *via* synthons derived from fatty acids. Such an account is presented in Section B.

CHART A.I

Important, naturally occurring, compounds prepared in the present work (section C) from Indian castor oil.

Compound	Related species
	Achroia grisella
	Lycorea ceres ceres
	Mamestra configurata
	Scotogramma trifolii
	Archips rosanus
	Choristoneura rosaceana
	Archips argyrospylus
	Platyonota stultana
	Grapholita molesta
	Bombyx mori
	Vaccenic acid
	Recifeiolide (Cephalosporium recifei)

B. BACKGROUND

A substantial portion of the energy stored in carbon frameworks is in the form of fatty acids. Their bio-synthesis and metabolism constitute one of the most important facets of energy storage and utilization by the living systems. Fatty acids, therefore, are ubiquitous in nature and they ought to serve, *inter alia*, as a rich source for very many varieties of synthons related to diverse structural frameworks. Surprisingly, in spite of this recognition, in contrast to other natural products, such as, carbohydrates, isoprenoids and alkaloids, the utilization of naturally occurring fatty acids for organic syntheses has, thus far, received scant attention. Indeed, there appears to be no review that illustrates possibilities in this direction. It was felt, therefore, that such an account would be a useful, timely and appropriate background to the present work. In view of the vastness of the area and the great difficulties relating to the identification of different types, the material presented in this Section is illustrative rather than

exhaustive, excepting for a fairly comprehensive literature coverage for a single year, namely, 1981, *via* the medium of Chemical Abstracts. Nevertheless, it is hoped that this background would be adequate in illustrating the possibilities of fatty acids derived synthons in organic syntheses. Parenthetically, in the following account, wherever the source for the starting synthon is not given, possible ways by which it could arise, from either readily available, naturally occurring, fatty acids, or synthons derived from them, are appended and connected to the citation by broken arrows.

Fatty Acids as a Source of Synthons related to Insect Sex Pheromones

Olefinic Synthons :

The insect sex pheromone, bombykol, of the species *Bombyx mori*, has been prepared *via* regioselective opening of epoxide related to methyl undec 10-enoate with acetylide (Chart B.I).[1] A key C-13 terminal oxirane again serves as an excellent precursor for the chiral δ-lactone related to a species of oriental hornet. The oxirane, in turn, can readily be related to methyl undec 10-enoate, a thermal fragmentation product of castor oil (Chart B.II).[2] A number of insect sex pheromones have been prepared from terminal π-systems derivable from fatty acids by cleavage to aldehyde followed by Wittig reaction (Chart B.III).[3]

CHART B.I

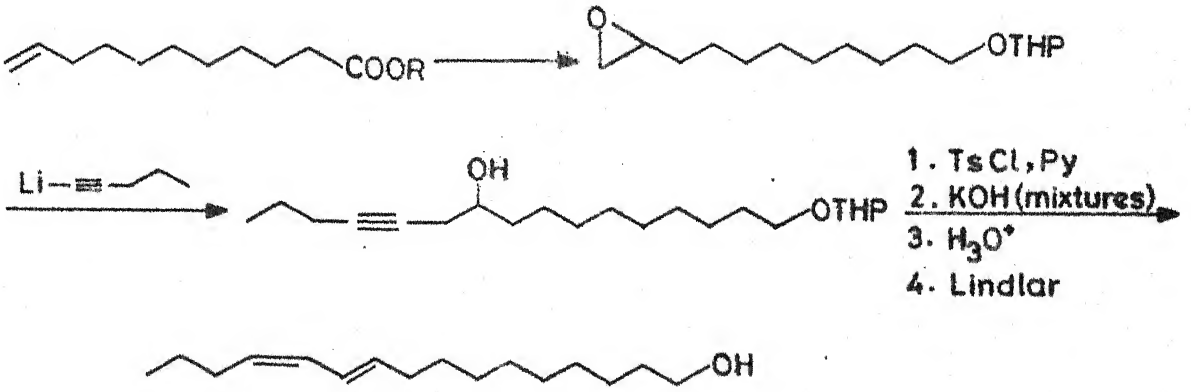


CHART B.II

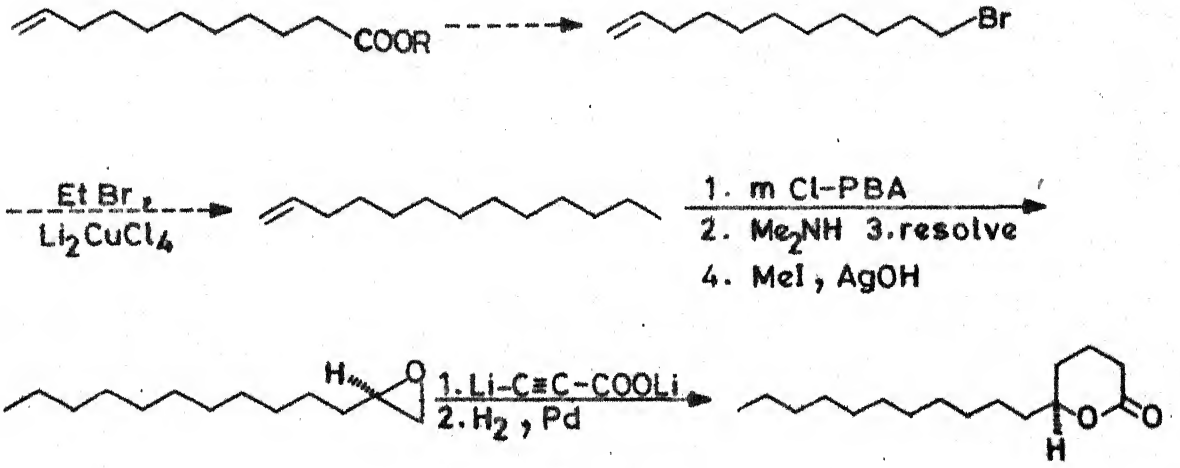
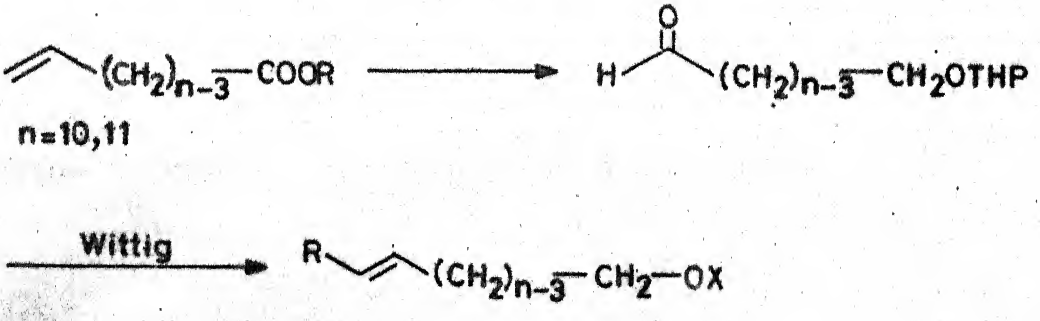


CHART B.III



Acetylenic Synthons :

Insect pheromones, generally, could be antithetically analysed in terms of the union of a head group, which carries a polar functional unit, and a hydrophobic tail fragment. The acetylide grouping has served as an excellent agent to bring about the combination of the head and tail moieties (Chart B.IV, Chart B.V).[4,5] A recently discovered, appealing, strategy for such a combination, useful for the synthesis of pheromones possessing multiple π-arrays, is by group transfer mediated by boranes. This can be illustrated with the synthesis of bombykol wherein the key step involves the transfer of a 1-pentynyl fragment to a synthon derivable from methyl undec 10-enoate (Chart B.VI).[6] This strategy also offers a general route to insect sex pheromones possessing E,E 1,3 diene units (Chart B.VII).[7] The key group transfer can also be brought about with Pd complexes, as illustrated with the synthesis of the pheromone related to Lobesia botrana (Chart B.VIII).[8] That the acetylene can serve as an attractive agent to bring about the combination of the two fragments is illustrated in Chart B.IX.[9] In this strategy, a Z-disposed CuLi π system, arising from the addition of an organo-lithio copper agent to acetylene, readily couples with a halide leading to pheromones possessing a Z π-unit.

CHART B.IV

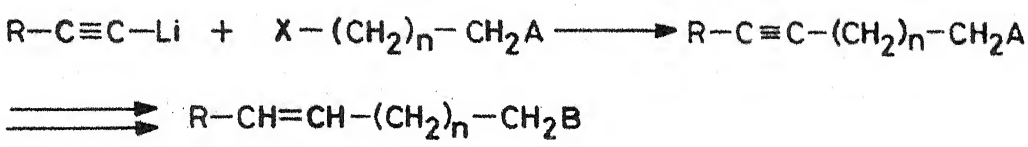


CHART B.V

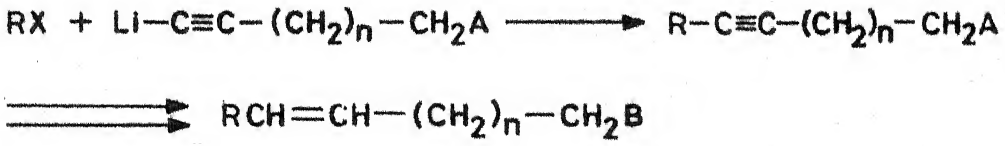


CHART B.VI

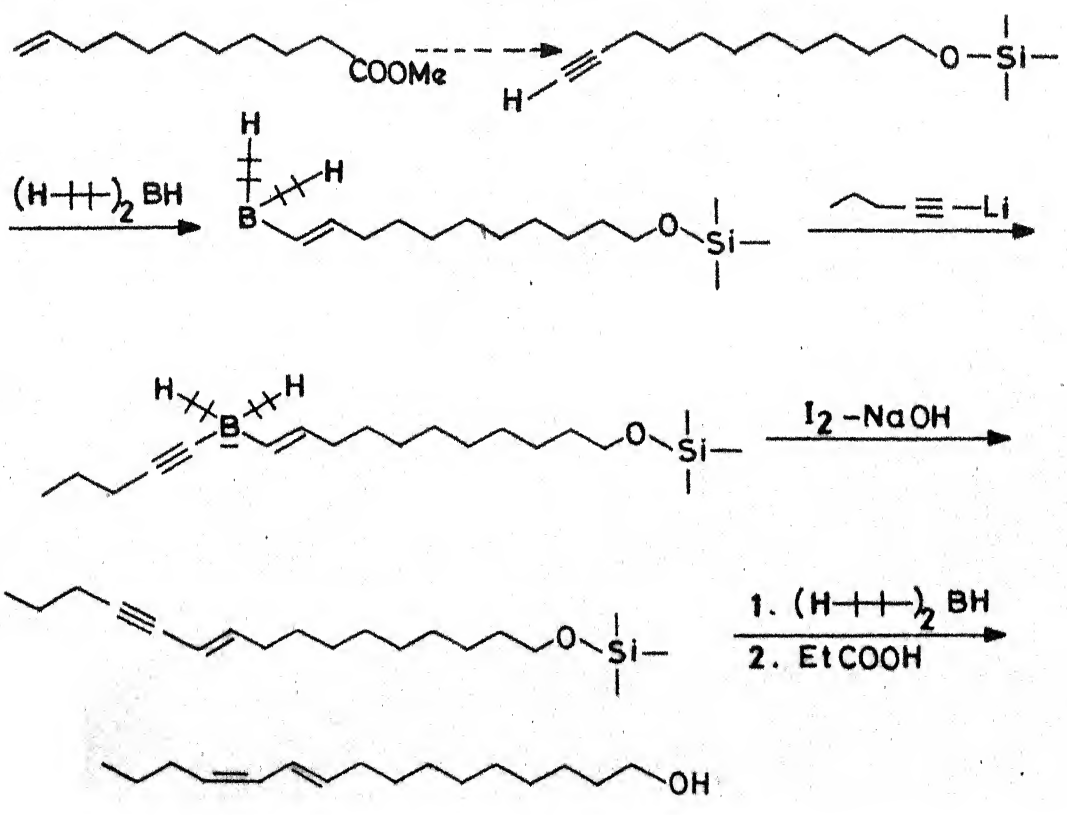


CHART B.VII

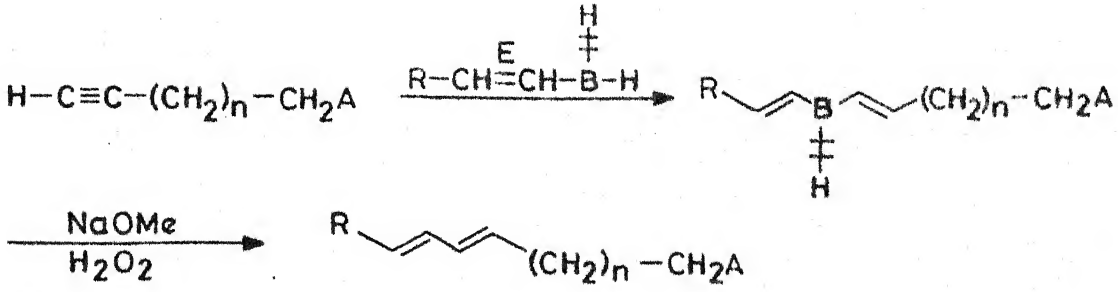


CHART B.VIII

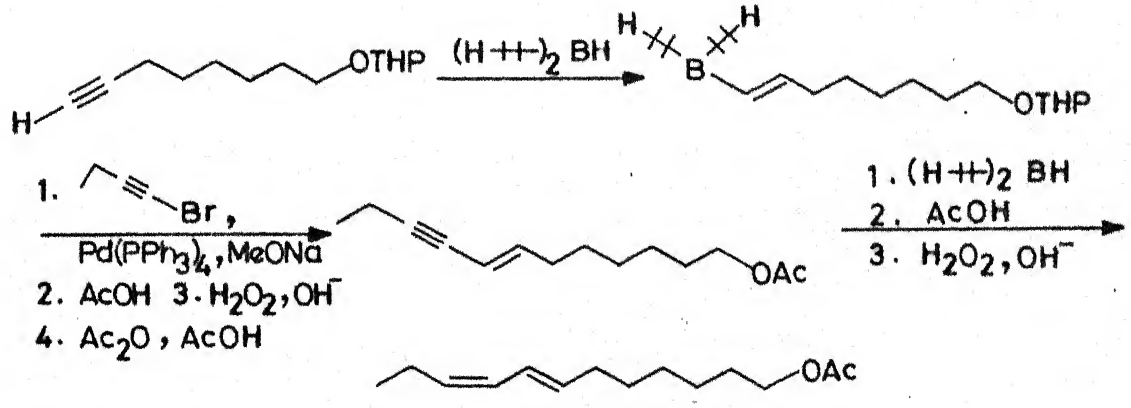


CHART B.IX

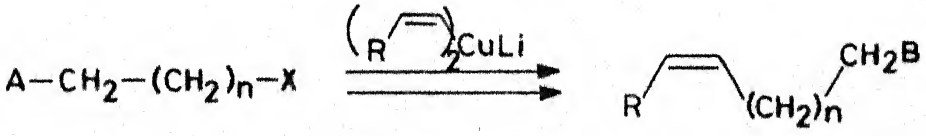
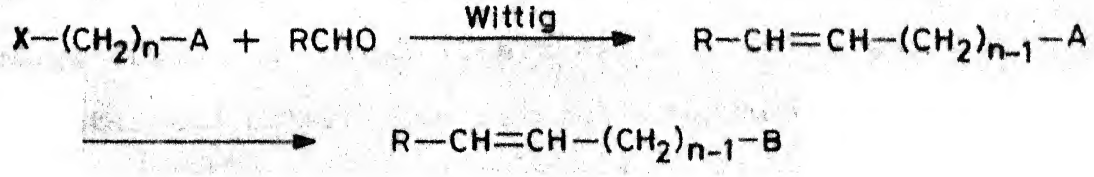


CHART B.X



Halide Synthons :

A rational comprehension of the factors which give rise to either the E or the Z double bond has led to a very popular method for the synthesis of insect sex pheromones by the Wittig reaction (Chart B.X).[10] Organometallic agents can be efficiently coupled with allylic halides in presence of the catalyst Li_2CuCl_4, thus, leading to the synthesis of insect sex pheromones (Chart B.XI).[11] C-C bond formation leading to the synthesis of pheromones has also been accomplished *via* nucleophilic displacement with phosphonate anions. This functional group could then be removed with LAH leading to, regioselectively, π -transposed systems (Chart B.XII).[12]

Oxo Synthons :

A number of insect sex pheromones have been prepared, *via* Wittig reaction, from oxo synthons readily available from fatty acids (Chart B.XIII).[13] Silicon containing synthons offer many advantages in syntheses. Thus, their conjugate bases can be stabilized and the tendency of the silicon residue to depart readily and its affinity to oxygen can be taken advantage of. These are illustrated in the very attractive synthesis of disparlure from n-undecanal (Chart B.XIV).[14] The generation of α,β - unsaturated esters from saturated precursors is a rather vexing problem. An excellent methodology is now available for

CHART B.XI

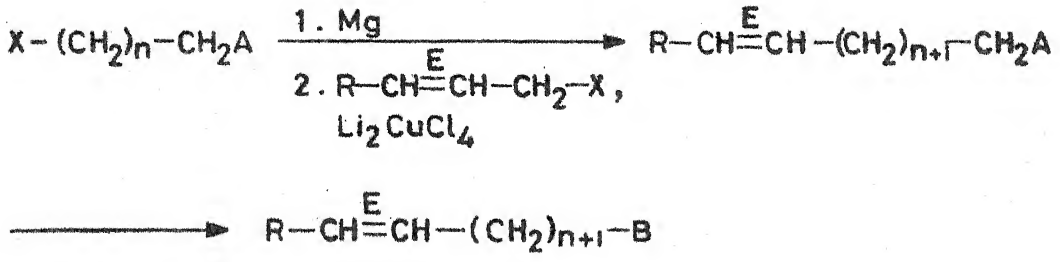


CHART B.XII

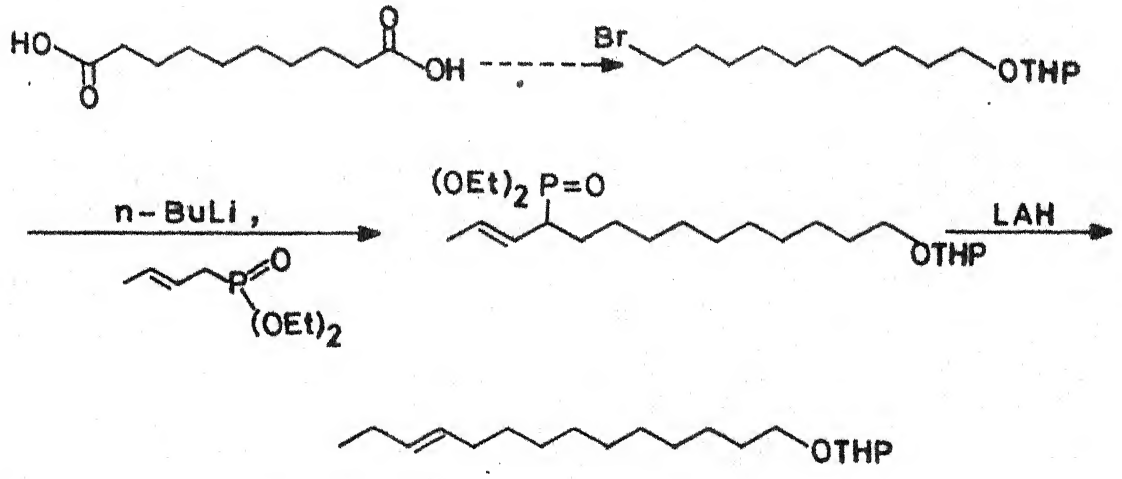


CHART B.XIII

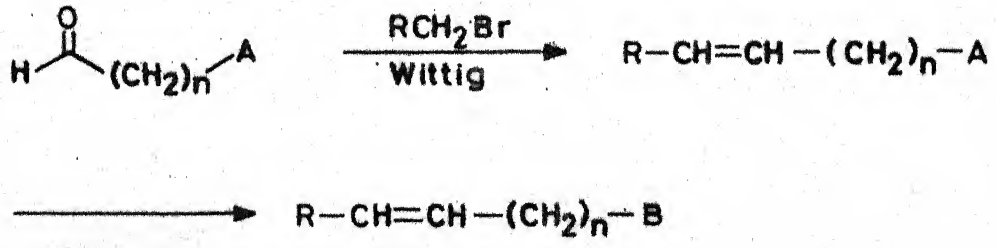


CHART B.XIV

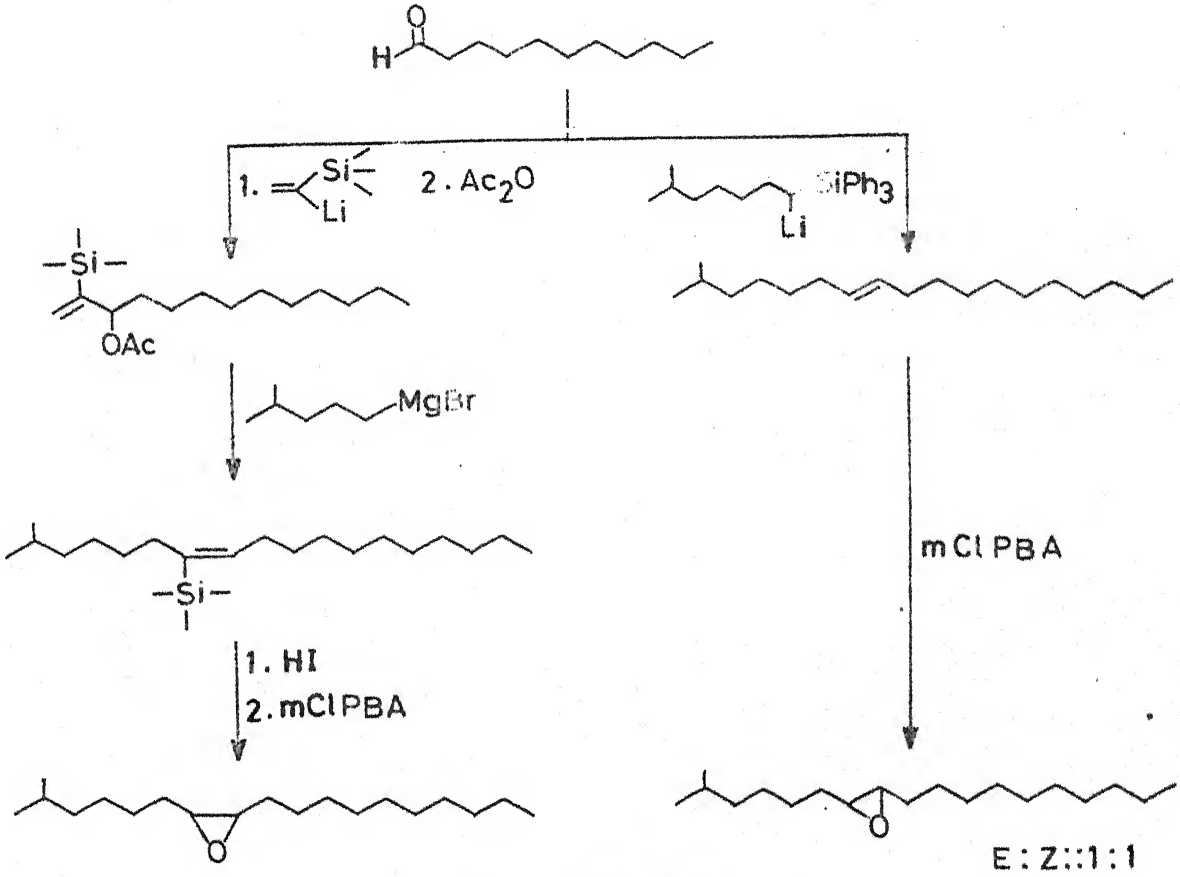
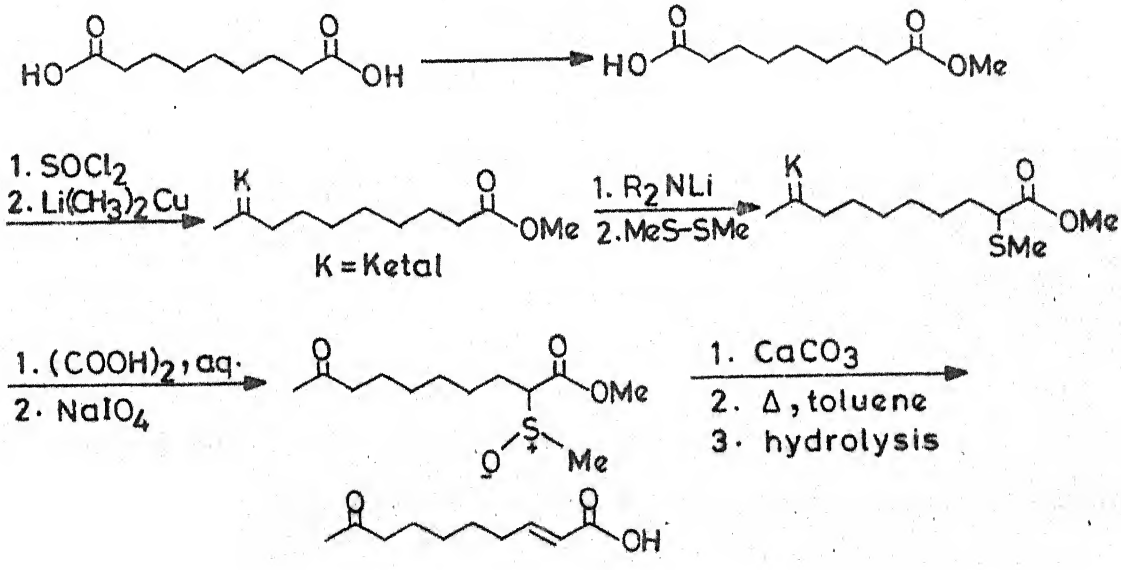


CHART B.XV



this transformation *via* elimination involving sulfoxides. This is illustrated with the transformation of methyl 9-oxo decanoate, available from azealic acid, to the queen bee pheromone (Chart B.XV).[15]

Fatty Acids as a Source of Synthons related to Prostaglandins

All prostaglandins can be considered, in principle, as derivatives of the hypothetical non-natural fatty acid, prostanoic acid. Notionally, prostaglandins are chirally and, or otherwise, functionalized prostanoic acids. Consequently, synthons derived from fatty acids which have been transformed to prostaglandins, or intermediates related to these, are either fragments of, or re-structured, naturally occurring fatty acids. For example, the head segment of oleic acid has been ingeniously incorporated in PGE_1 *via* nucleophilic addition to a highly functionalized chiral aldehyde (Chart B.XVI).[16] PGE_1 has also been prepared from methyl undeca 8,10-dienoate by cyclo-addition followed by re-organisation (Chart B.XVII).[17] The first synthesis of PGE_1 involved, as the primary step, the Michael addition of a nitronate to 1-cyano 9-oxo non 7-ene, readily derivable from methyl undec 10-enoate (Chart B.XVIII).[18]

Castor oil bears a striking resemblance to $PGF_1{}^{\alpha}$ and the re-structuring of the former to the latter has been accomplished. Additionally, the strategy employed for this transformation led

CHART B . XVI

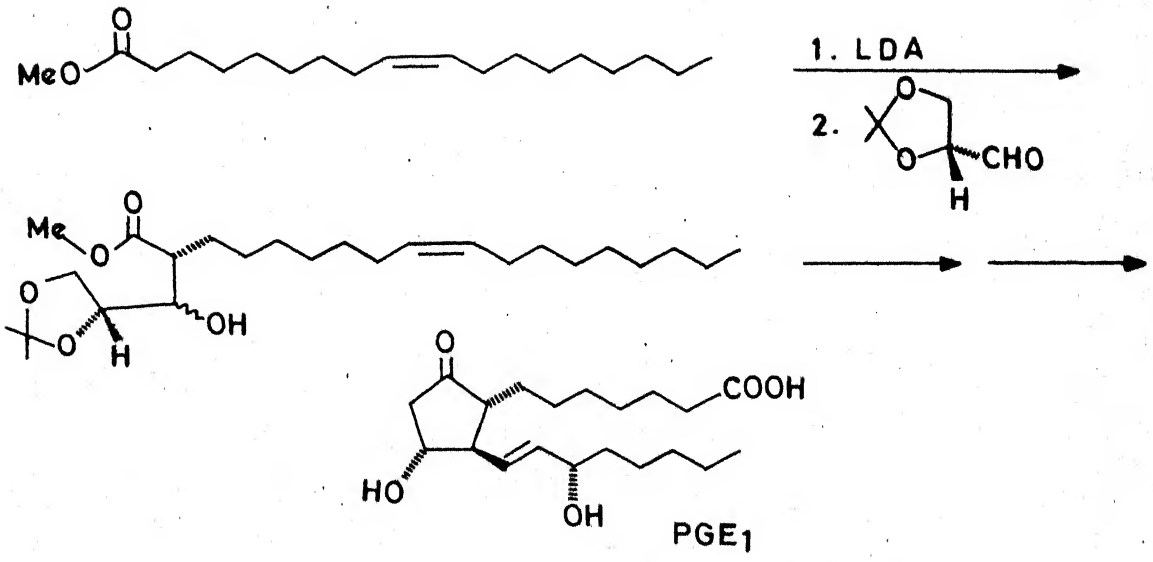


CHART B . XVII

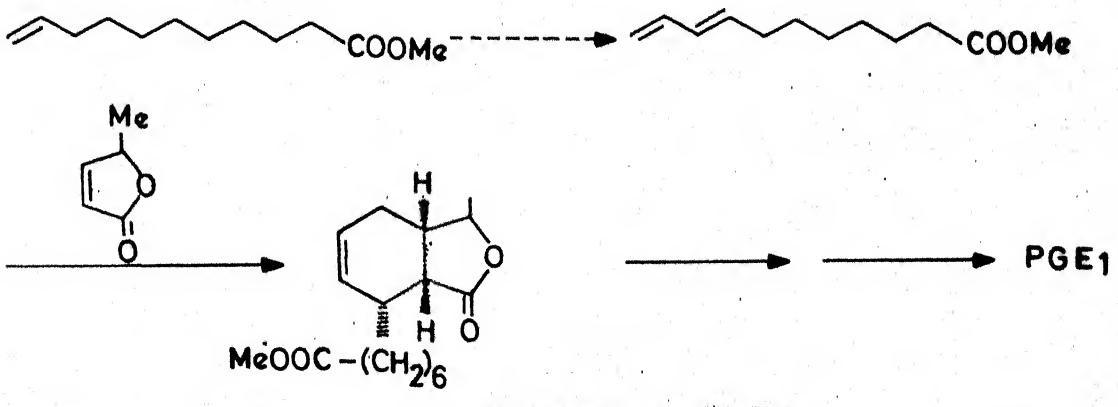
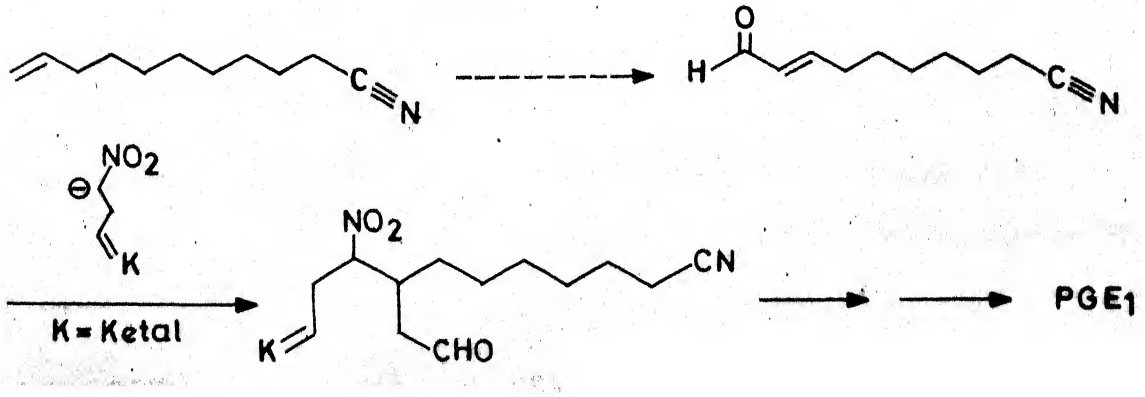


CHART B . XVIII



to a route for etheno PGH_1 (Chart B.XIX).[19] Ethyl 9-cyano non 8-enoate and 1-cyano 8-nitro oct 7-ene, which can now be prepared from sebacic acid by procedures developed in the present work, are synthons which have been transformed, by key 4 + 2 additions, to, respectively, $PGF_1\alpha$ and PGE_1 (Chart B.XX, Chart B.XXI).[20,21] Enrichment of functionality on diethyl sebacate *via* alkylation with ethyl cyanoacetate is another strategy that has been used for synthesis of PGE_1 (Chart B.XXII).[22] By a similar method, dimethyl 9-oxo undecanoate has been transformed to $PGF_1\alpha$ (Chart B.XXIII).[23] The identification of 1-(6'-carbomethoxy hexyl)-cyclopent 1-enone as a prostanoid synthon has led to the discovery of several routes to this enone, the most important ones of which originate from methyl undec 10-enoate and traumatic acid (Chart B.XXIV).[24] The regioselective opening of alkoxy cyclopropyl ketones forms the key strategy in the transformation of azealic acid to the above cyclopentenone. Interestingly, the cyclopropyl system was generated from a diazoketone by carbenic addition to n-butyl vinyl ether (Chart B.XXV).[25] The cyclopentenone system has been constructed, in a novel manner, by key addition of a cyclopropane equivalent to methyl undec 9-ynoate which can be readily prepared from undec 10-enoic acid (Chart B.XXVI).[26]

An equally versatile prostanoid synthon is 3-(6'-carbomethoxy hexyl)-cyclopentane 1,2,4 trione, whose chief attraction

CHART B.XIX

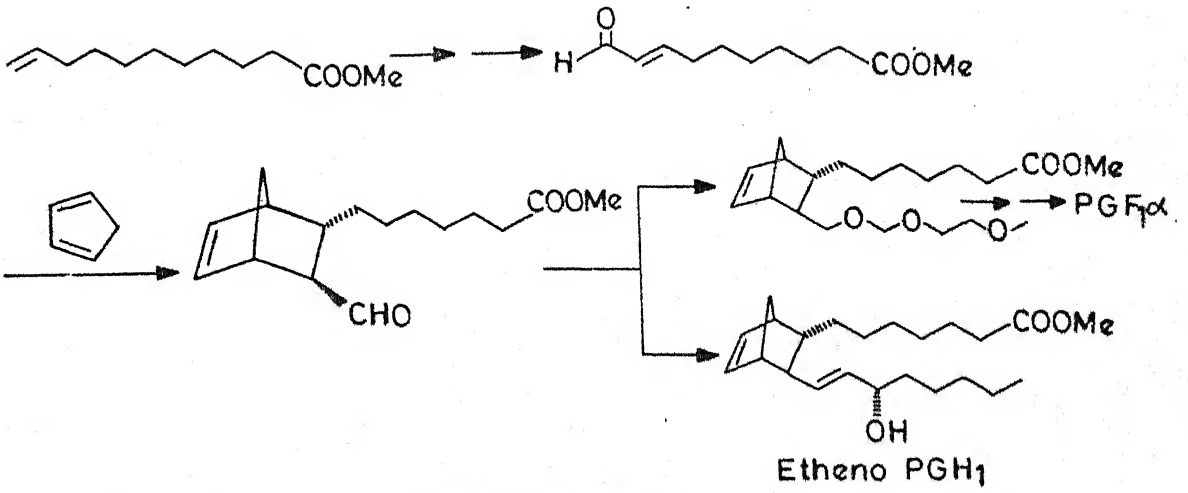


CHART B.XX

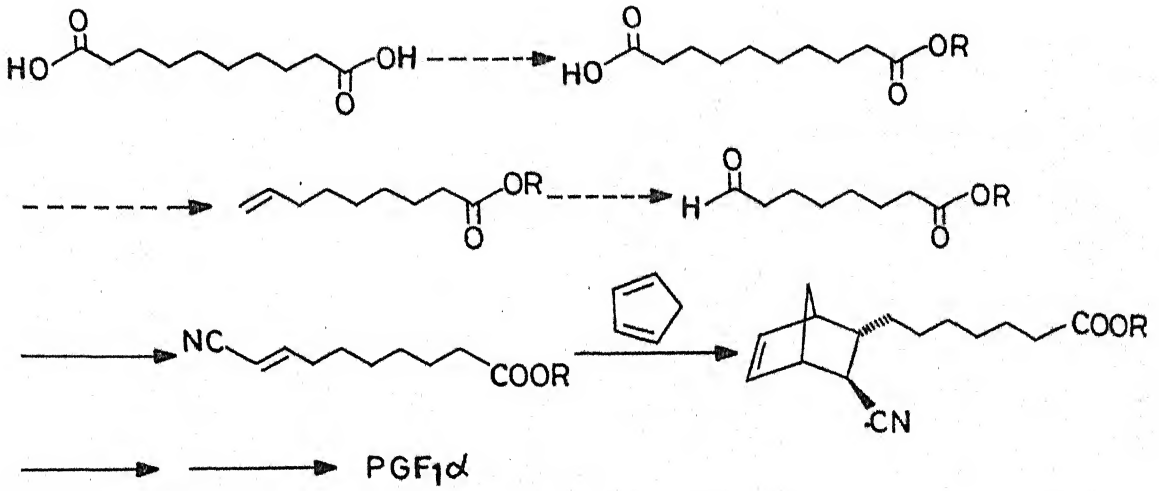


CHART B.XXI

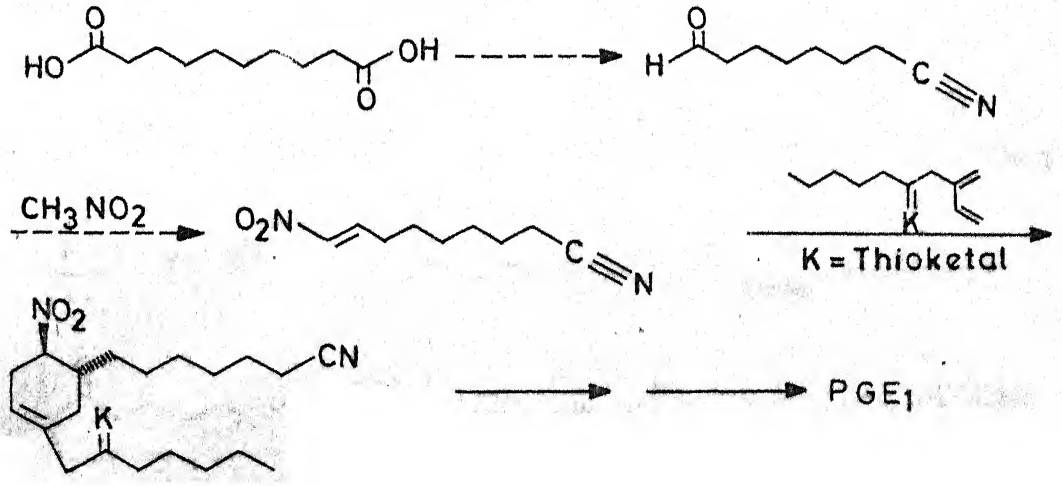


CHART B.XXII

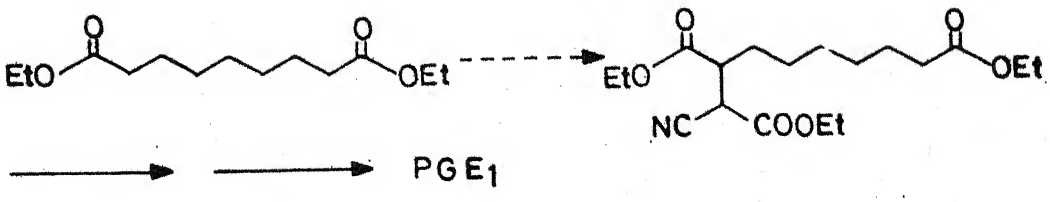


CHART B.XXIII

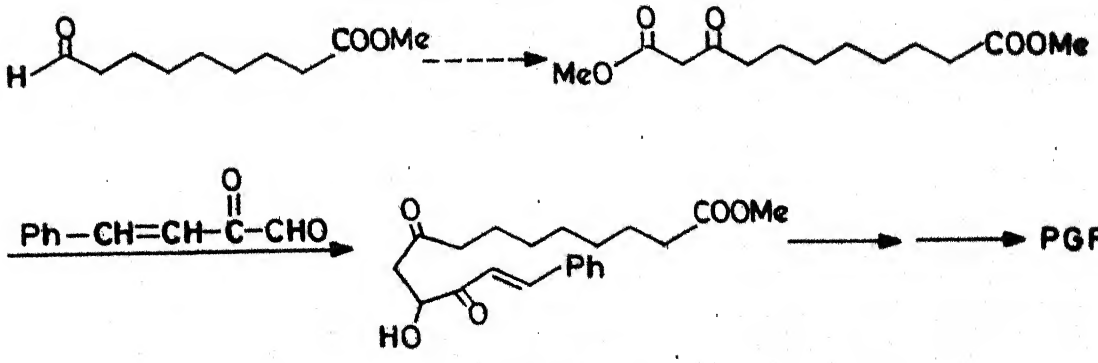


CHART B.XXIV

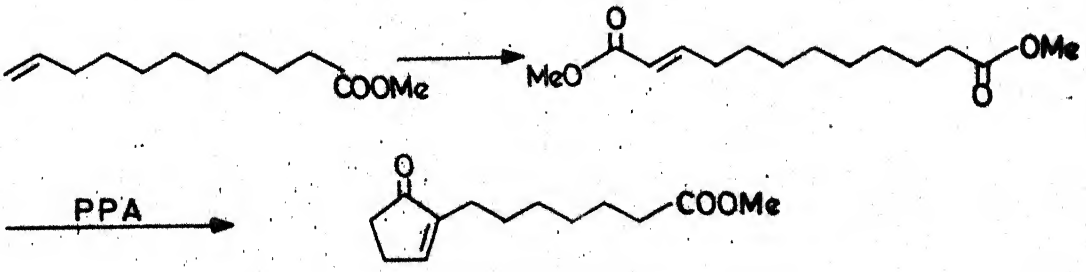


CHART B.XXV

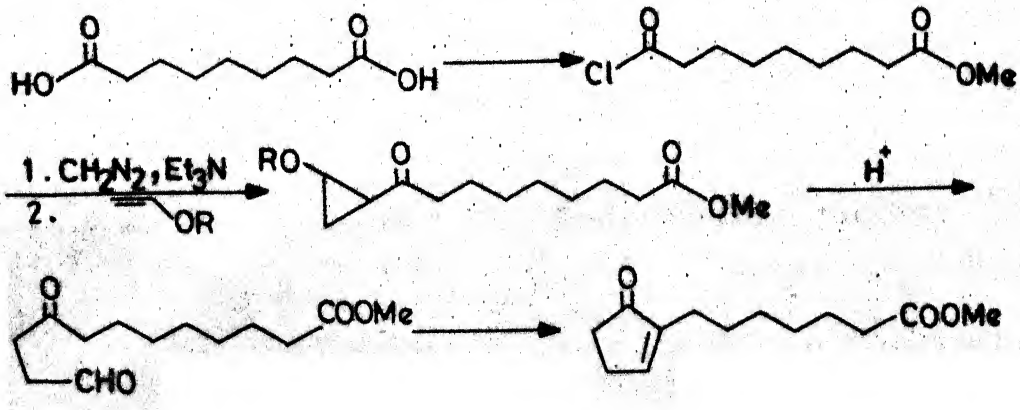


CHART B.XXVI

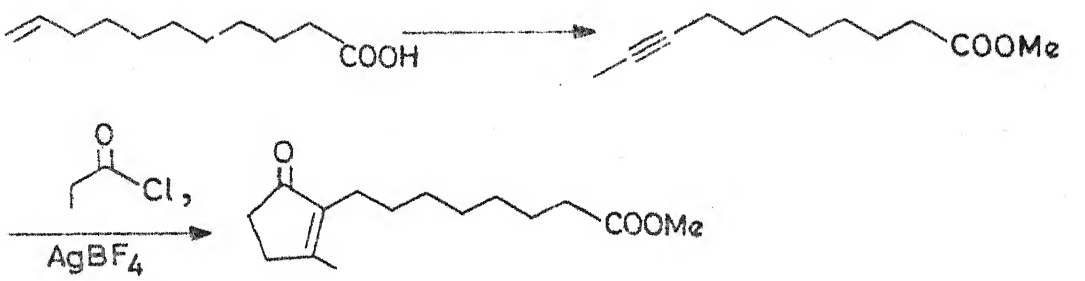


CHART B.XXVII

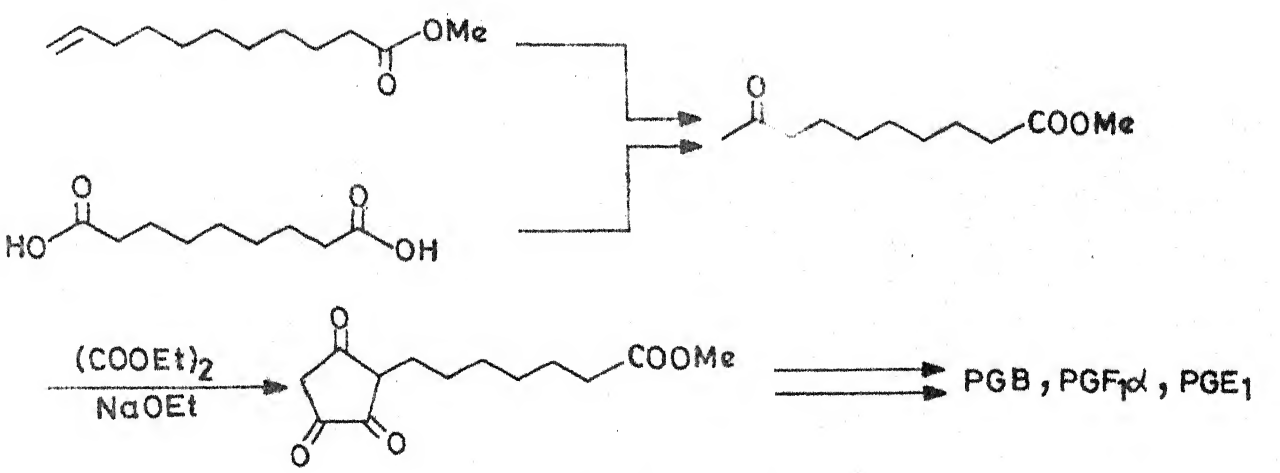
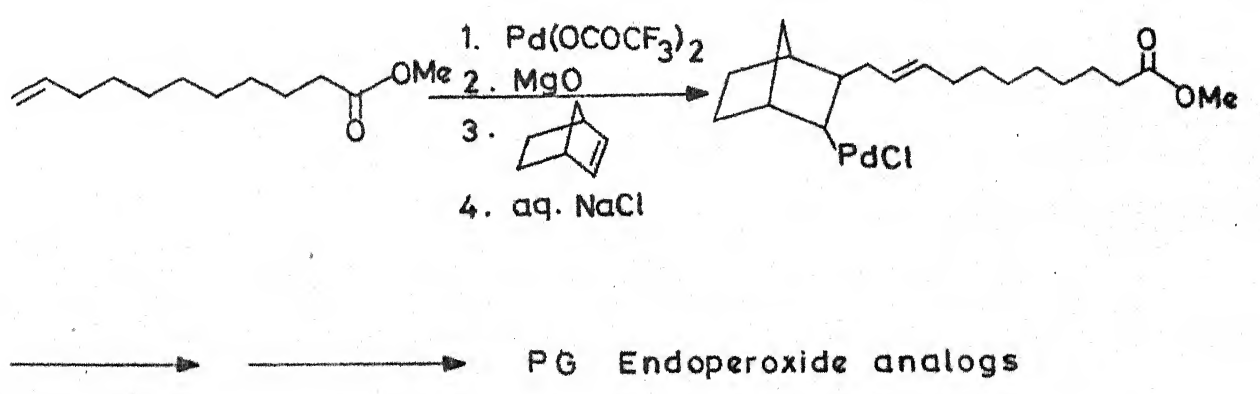


CHART B.XXVIII



being the ease with which the 1-carbonyl function can be reduced asymmetrically to the (R) alcohol with Dipodascus uninucleatus. The synthesis of the trione has been achieved from the readily available methyl undec 10-enoate or azealic acid (Chart B.XXVII).[27] Synthons derived from fatty acids have been used in the preparation of various prostaglandin analogs, a noteworthy illustration being the synthesis of PG endoperoxide analogs via an unusual addition of methyl undec 10-enoate to norbornene mediated by Pd reagents (Chart B.XXVIII).[28] The γ,δ-unsaturated alcohol unit in castor oil can be quite easily transformed to the 1,4-diketone, the latter, on aldol condensation, gives rise to disubstituted cyclopentenones which bear a striking resemblance to prostaglandin (Chart B.XXIX).[29] Di-oxa prostaglandins can also be prepared from methyl undec 10-enoate (Chart B.XXX).[30]

Fatty Acids as a Source of Synthons for Unusual and Rare Fatty Acids

The established metabolic pathways in living systems exhibit a sharp preference for the synthesis and storage of a selected handful of fatty acids. On the other hand, a variety of fatty acids, not favoured by common metabolic pathways, play a vital role in living systems. The synthesis of such rare fatty acids constitutes a significant facet of the art in organic synthesis and it is becoming increasingly clear that the best

CHART B.XXIX

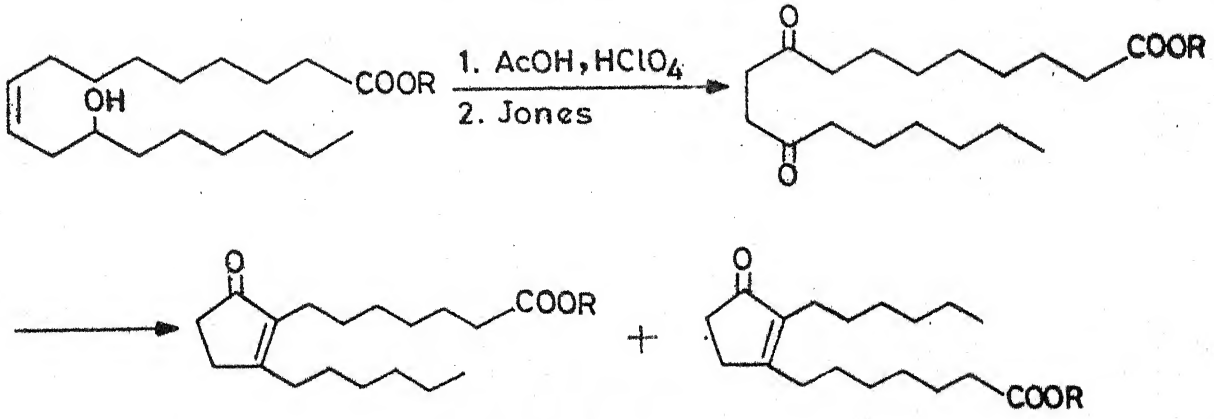


CHART B.XXX

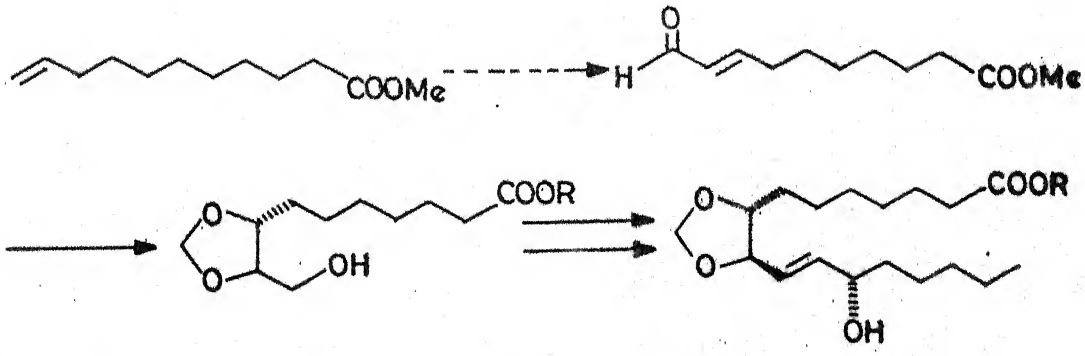
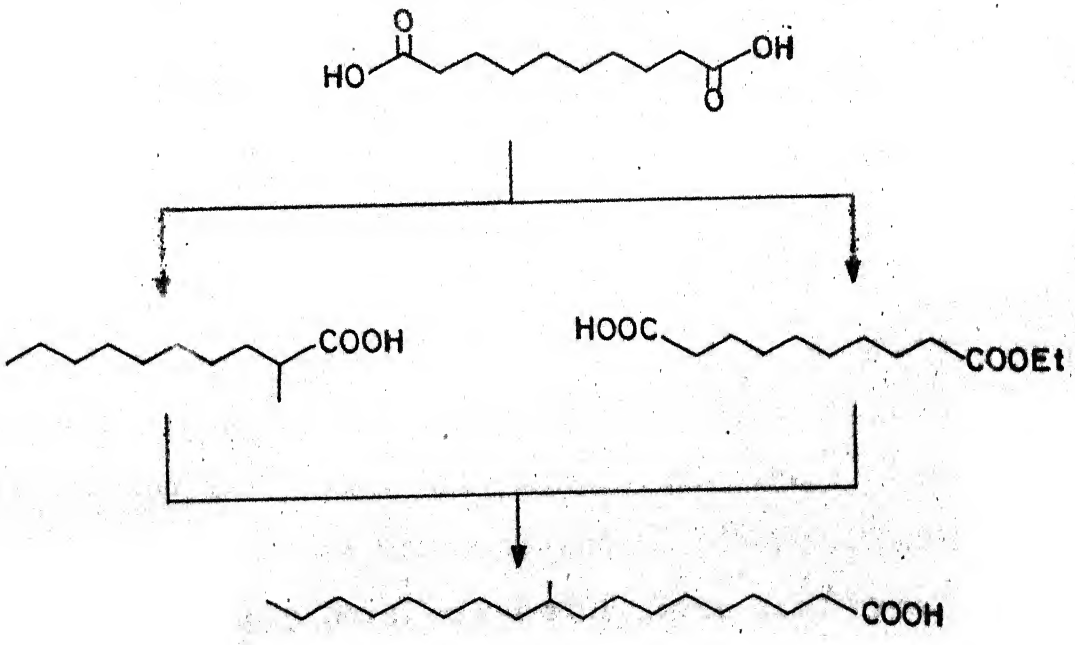


CHART B.XXXI



methodology for their preparation is from synthons derived from readily available fatty acids.

Tuberculostearic acid, 10-methyl octadecanoic acid, is a major lipid constituent of tubercle bacilli. This acid can readily be prepared from sebacic acid involving electrolytic coupling (Chart B.XXXI).[31] The elongation of the methylene chain of synthons from readily available fatty acids is a strategy commonly employed for the preparation of unusual fatty acids. Three different and interesting methodologies are illustrated in Chart B.XXXII,[32] Chart B.XXXIII,[33] and Chart B.XXXIV.[34] A lipid carrying a terminal hydroquinone unit has been prepared in a very elegant fashion *via* diborane mediated union of methyl undec 10-enoate and quinone (Chart B.XXXV).[35]

It is of interest that chaulmoogra oil, a fatty acid glyceride, has been used for centuries in India and China for treatment of the two diseases caused by fat encapsulated acid-fast bacteria, leprosy and tuberculosis. The glycerides are probably converted in the body to the free fatty acid which is the active agent. Chaulmoogric acid, a major component of the oil has been prepared by the union of cyclopentenyl acetic acid with tridecane 1,13-dioic acid monoester. The latter can readily be prepared from methyl undec 10-enoate (Chart B.XXXVI).[36] The C-22 olefinic erucic acid, the major fatty acid present in

CHART B.XXXII

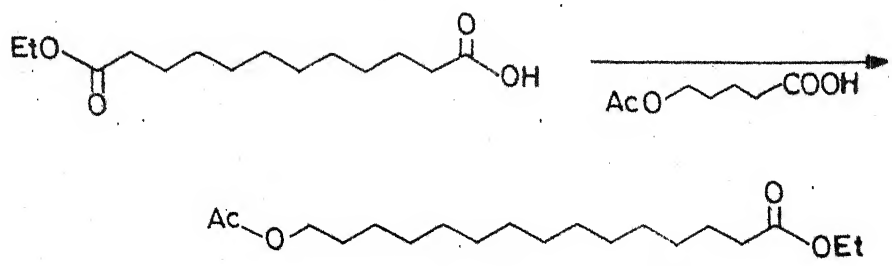


CHART B.XXXIII

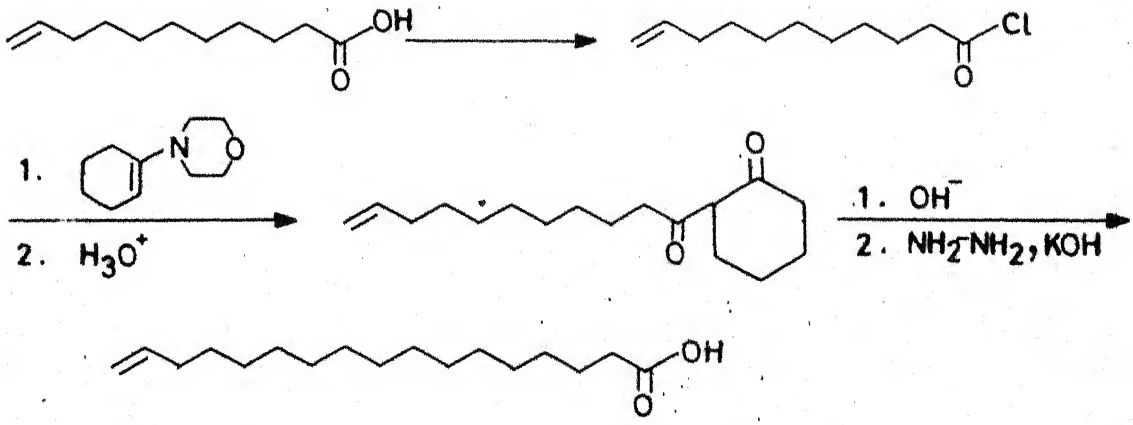


CHART B.XXXIV

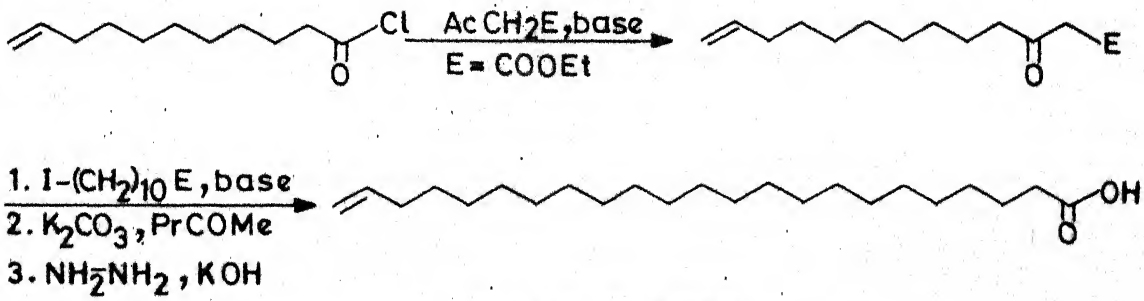


CHART B.XXXV

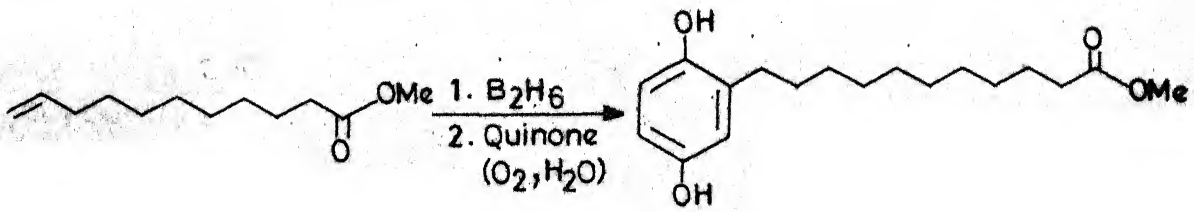


CHART B.XXXVI

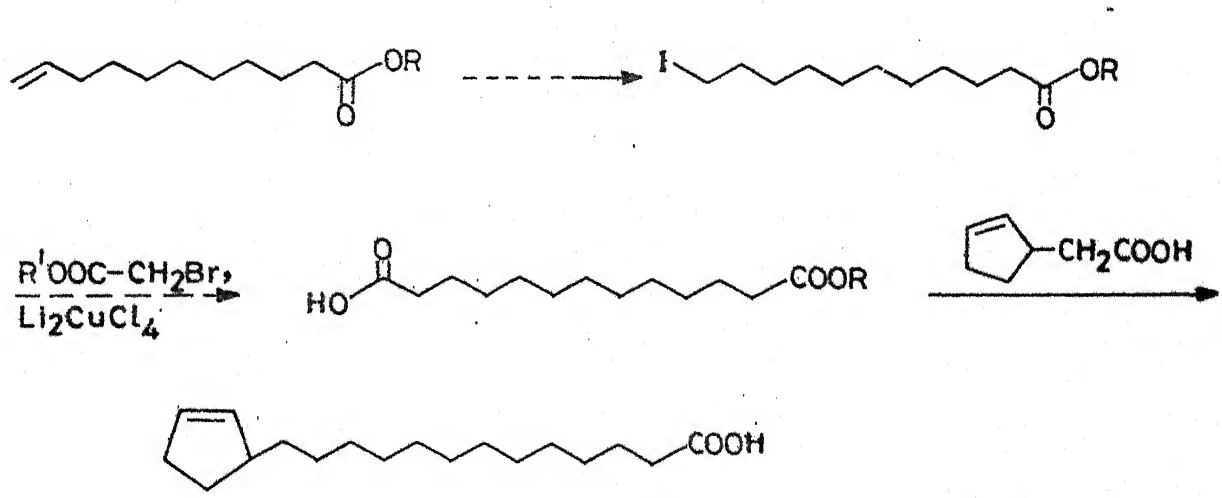


CHART B.XXXVII

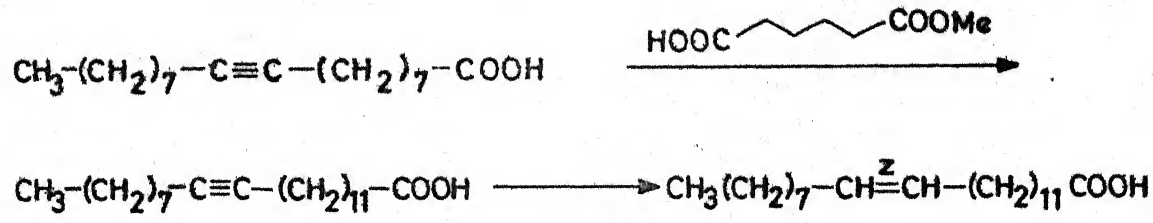
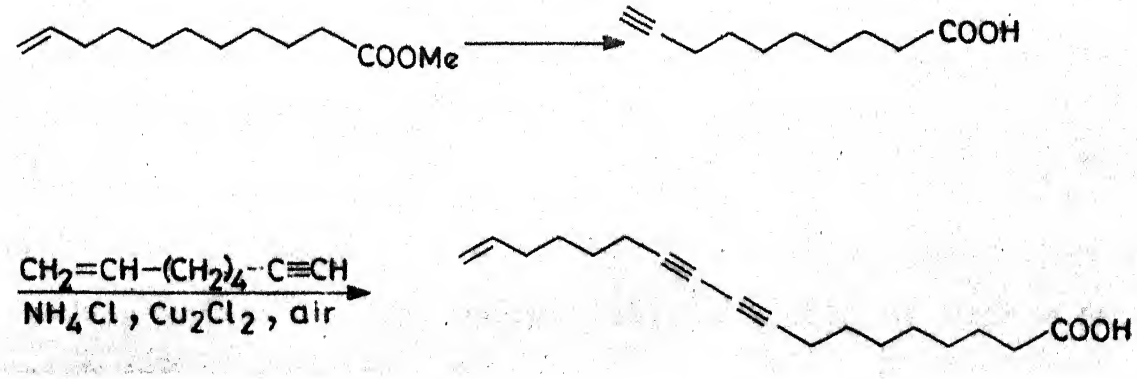


CHART B.XXXVIII



mustard seeds, has been prepared by homologation of stereolic acid involving the intermediacy of another, naturally occurring fatty acid, behenolic acid (Chart B.XXXVII).[37] Methyl undec 10-enoate is a good precursor for the di-acetylenic, isanic acid (Chart B.XXXVIII).[38] Lamenallenic acid, a naturally occurring allenic fatty acid, has been prepared from undec 10-enoic acid. A key feature of the synthesis is the generation of the allenic unit by reduction of a conjugated enyne system with LAH (Chart B.XXXIX).[39] Traumatic acid, 1,12-dodec (E) 2-ene dioic acid, is a plant constituent which induces division and extension of plant cells. The use of this for prostanoid synthesis has been illustrated (vide supra). An exceptionally practical route to traumatic acid involves radical induced addition of CCl_4 to undec 10-enoic acid followed by the $-CCl_3 \longrightarrow -COOH$ change and elimination (Chart B.XL).[40,24c]

Royal jelly, the sole food for the queen bee larvae and the adult queen, consists of carbohydrates (15%), proteins (31%) and lipids (15%), in addition to a number of vitamins and other growth factors. Royal jelly acid is the major component of the lipids. 10-Hydroxy dec (E) 2-enoic acid, the royal jelly acid, has been prepared from undec 10-enoic acid (Chart XLI).[41] Methyl undec 10-ynoate, easily available from methyl undec 10-enoate, forms a versatile organomercurial, on treatment with $R_2BH + HgCl_2$, which can be transformed to a variety of compounds (Chart B.XLII).[42]

CHART B.XXXIX

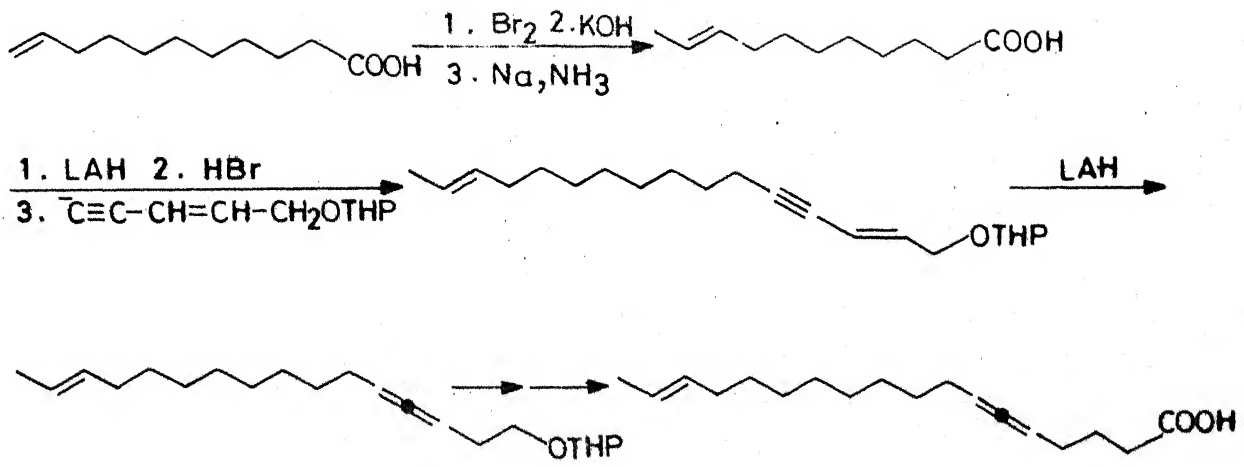


CHART B. XL

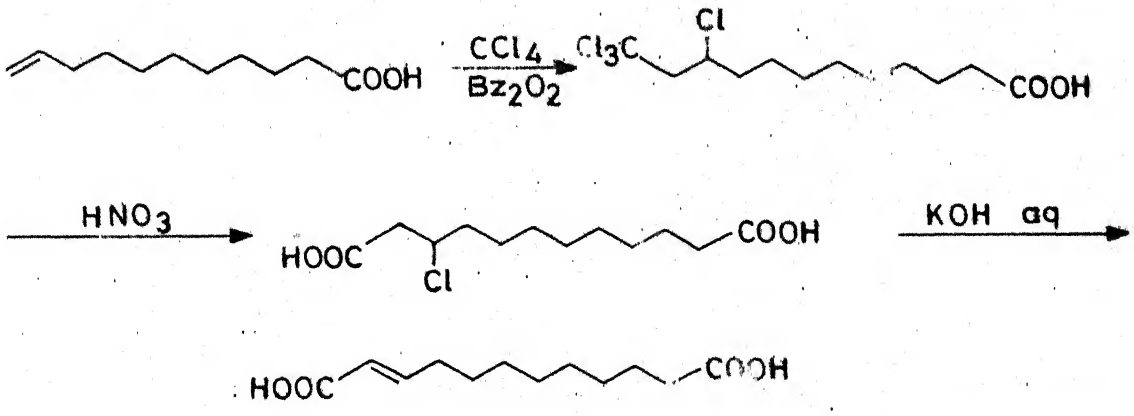


CHART B.XLI

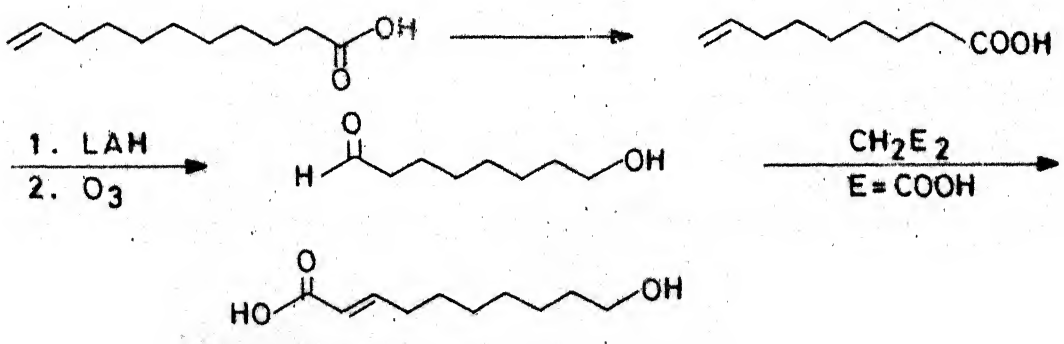


CHART B.XLII

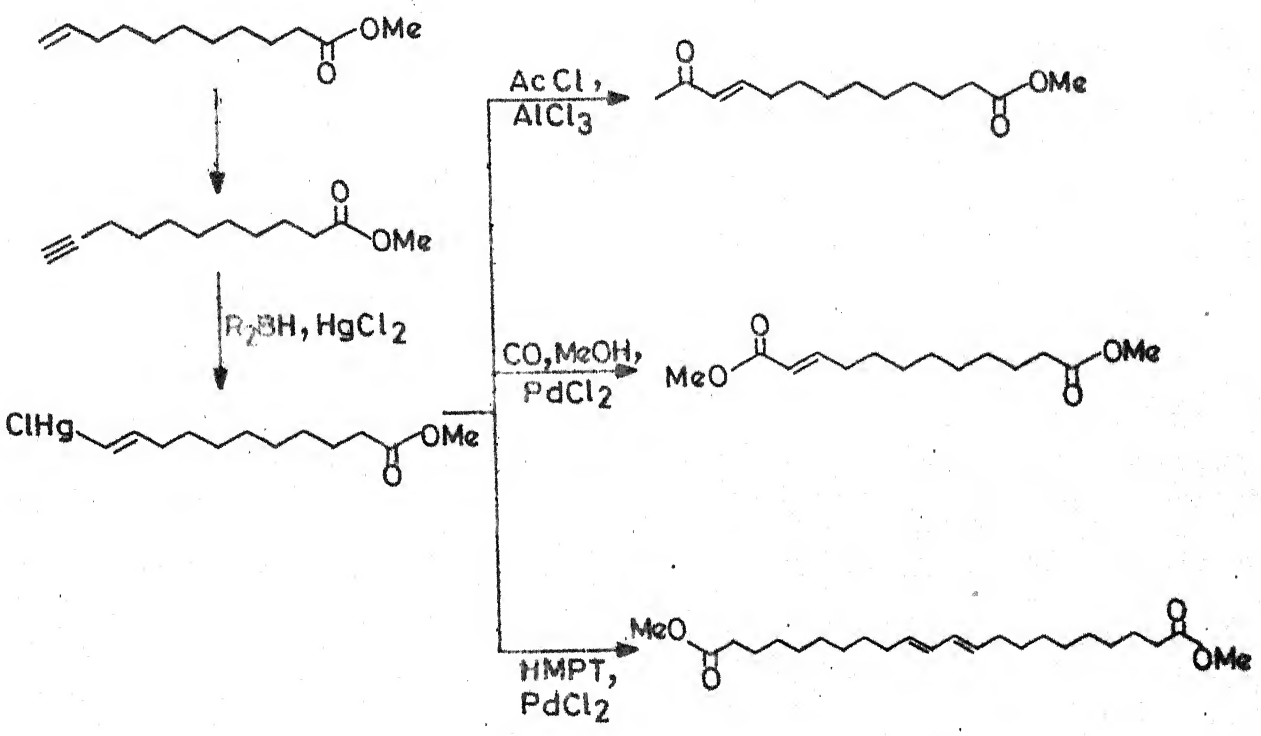
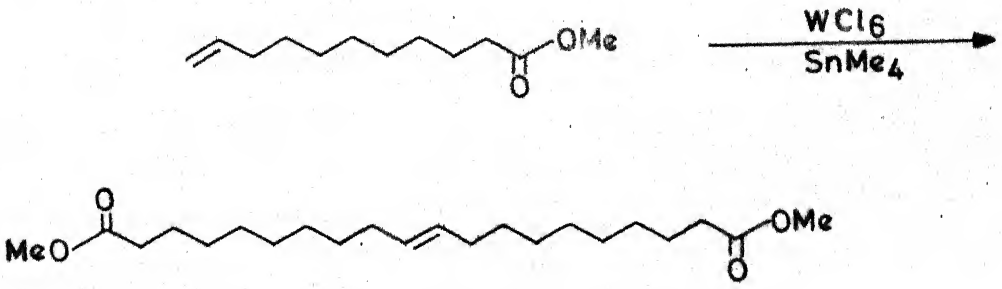


CHART B.XLIII



Perhaps the most significant development in the area of fatty acids is transformations brought about by metathetic processes. A recent understanding of the mechanistic pathways involved in these changes, coupled with the discovery of a variety of appropriate reagents and the development of techniques to effect a ready separation of the products, have very vastly increased the synthetic scope of this powerful method. A simple and apt illustration of this process is the ready metathetic transformation of methyl undec 10-enoate to dimethyl eicosa (E) 10-en dioate (Chart B.XLIII).[43] Nonanal, a degradation product of oleic acid, has been transformed to tetrahydrocerulenin (Chart B.XLIV).[44]

Metabolic pathways could be expected to undergo changes during dietary stress and recently a series of rare furanoid fatty acids have been isolated from aquatic species deprived of proper nutrition. A surprising correlation between these rare fatty acids and ricinoleic acid has been discovered recently. Thus, methyl ricinoleate is readily transformed to the above described furan containing fatty acids (Chart B.XLV).[45] A very interesting reaction of ricinoleic acid is its transformation to a lactone containing fatty acid with CO + H_2SO_4 (Chart B.XLV).[46]

Fatty Acids as a Source of Synthons for Macrocyclic Systems

The synthetic power of the metathesis reaction is best

CHART B.XLIV

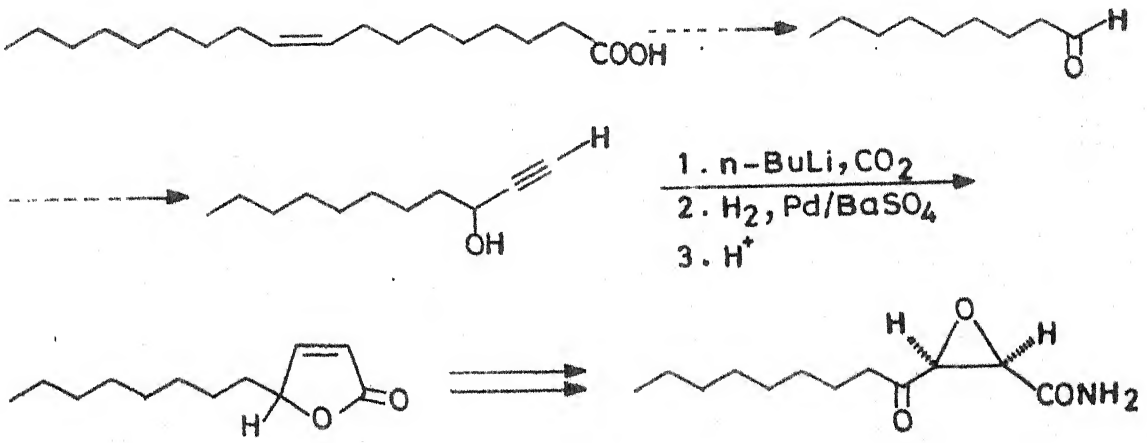
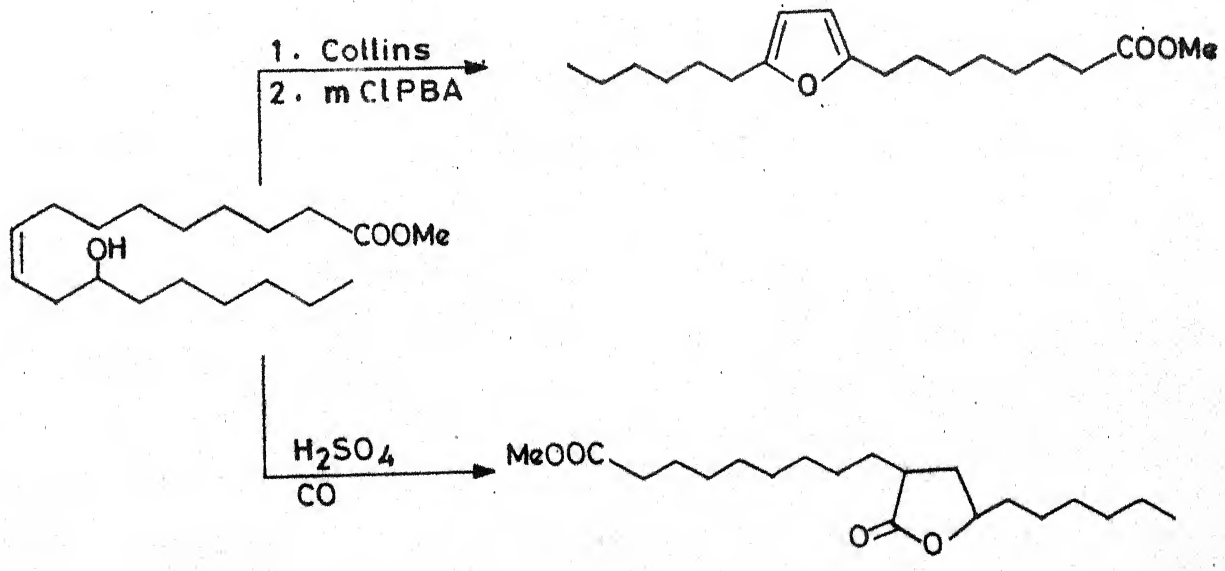
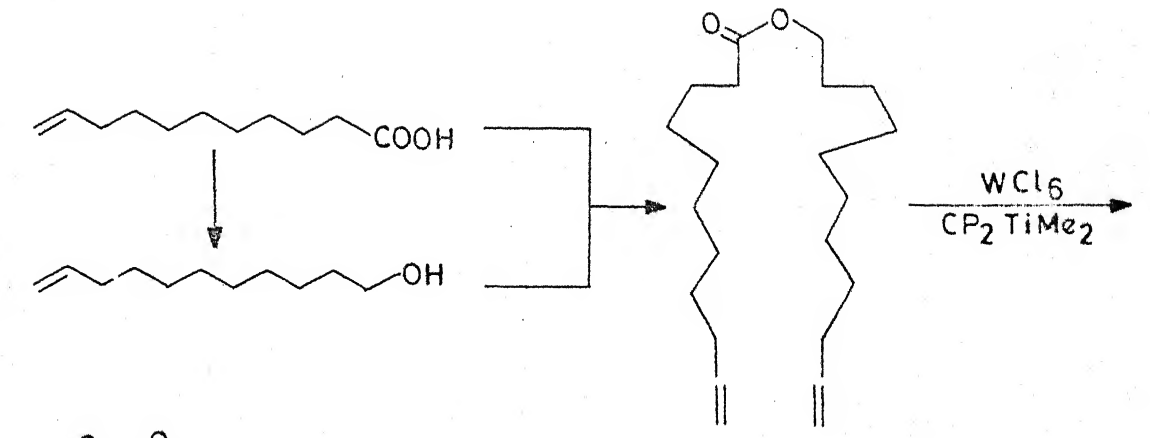


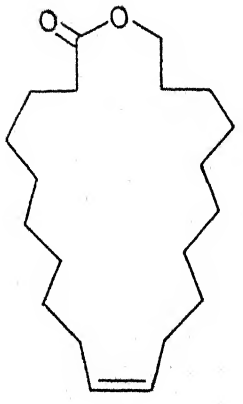
CHART B.XLV



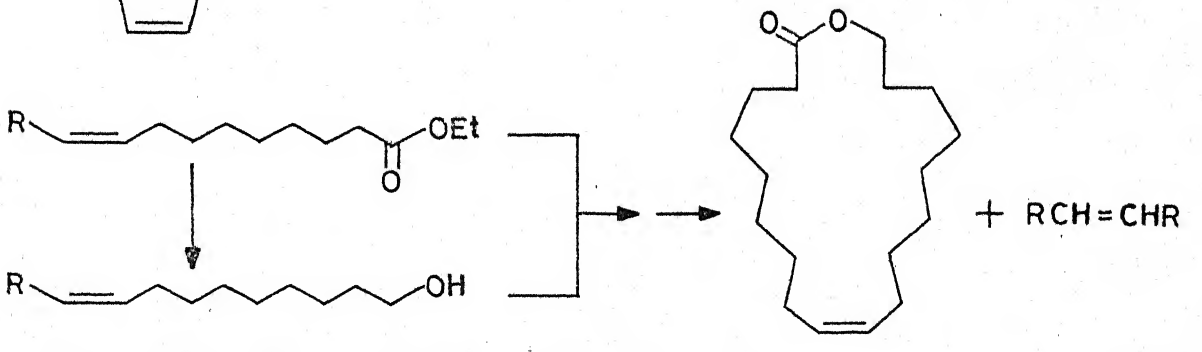
illustrated with the formation of the C-20 macrocyclic lactone on treatment of 10'-undecenyl undec 10-enoate with WCl_6-Cp_2TiMe_2. A similar set of reactions with oleyl oleate leads smoothly to a C-18 macrocyclic lactone and octadec 9-ene (Chart B.XLVI).[47] The musk-like odour of several seed oils is due to the presence of, in very small amounts, macrocyclic lactones. The synthesis of one of these, namely, iso-ambrettolide, a C-16 lactone has been accomplished from chloro undec 10-ene (Chart B.XLVII).[48] The ω-hydroxy carboxylic system, a requisite for macrocyclic lactones, can be created from appropriate organo copper reagents and β-propiolactone. Thus, 12-methoxy dodecyl magnesium bromide reacts with β-propiolactone in presence of Cu leading to 15-methoxy pentadecanoic acid which can be readily cyclised to exaltolide (Chart B.XLVIII).[49] An ingenious method has been recently discovered for the preparation of macrocyclic lactones from fatty acids derived synthons, wherein a 2-methyl oxazole unit serves, not only as the recipient of the lipid unit, but also, as a precursor to a highly activated amide. The strategy involved in this is illustrated with the synthesis of 13-tridecanolide (Chart B.XLIX).[50] Ricinelaidic acid has been cyclised to a C-12 macrocyclic lactone that bears a striking resemblance to recifeiolide (Chart B.L).[51] Macrocyclic lactones that incorporate a peri phenyl bridge have been prepared by an unusual cleavage of oxetanes resulting from photochemically induced, intramolecular cyclo-addition of 10-undecenoic esters (Chart B.LI).[52]

CHART B.XLVI



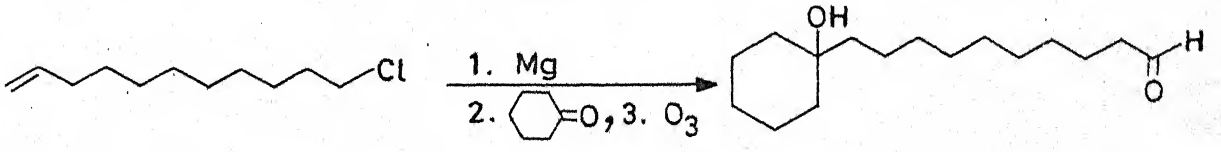


+ $H_2C{=}CH_2$



R = n-C_8H_{17}

CHART B.XLVII



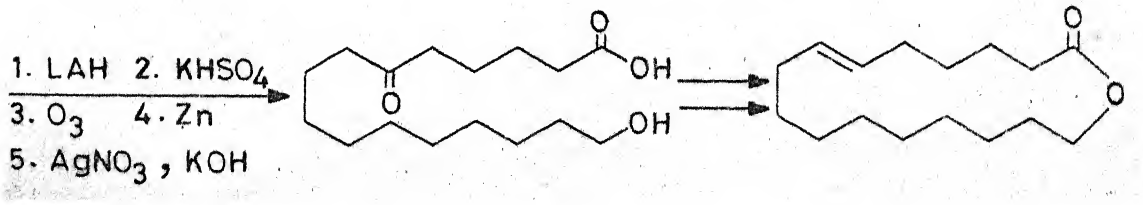


CHART B. XLVIII

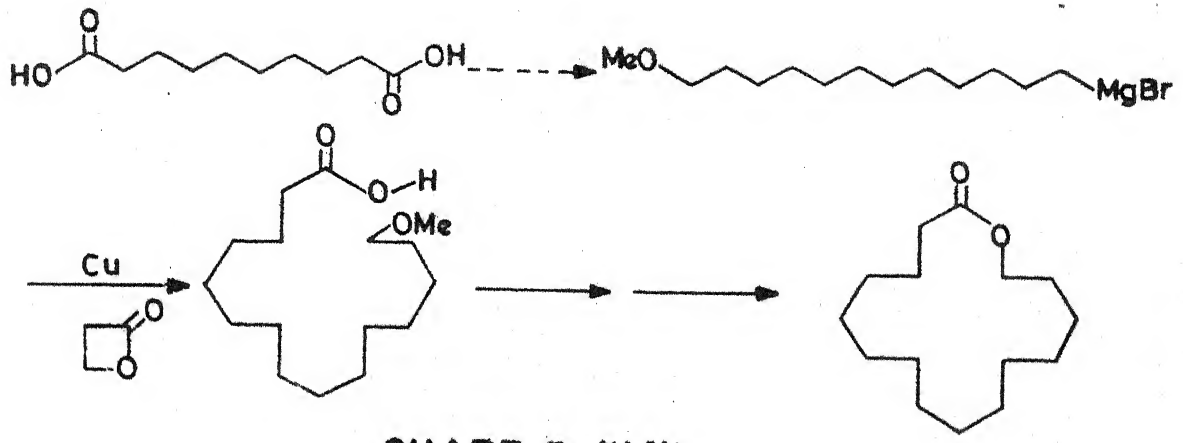


CHART B. XLIX

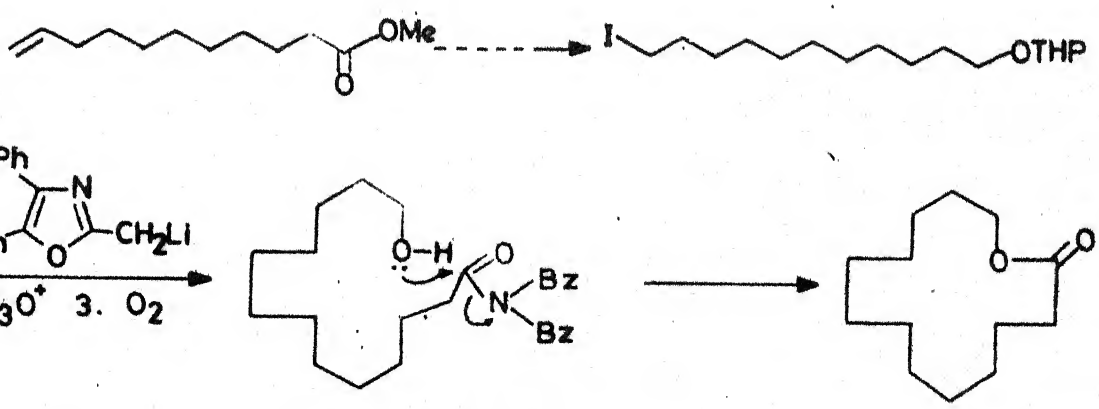


CHART B. L

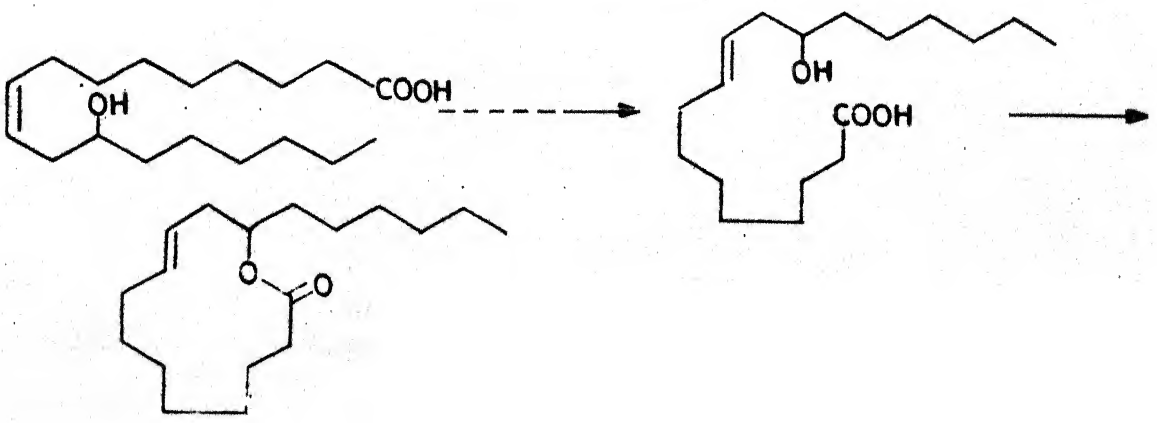


CHART B. LI

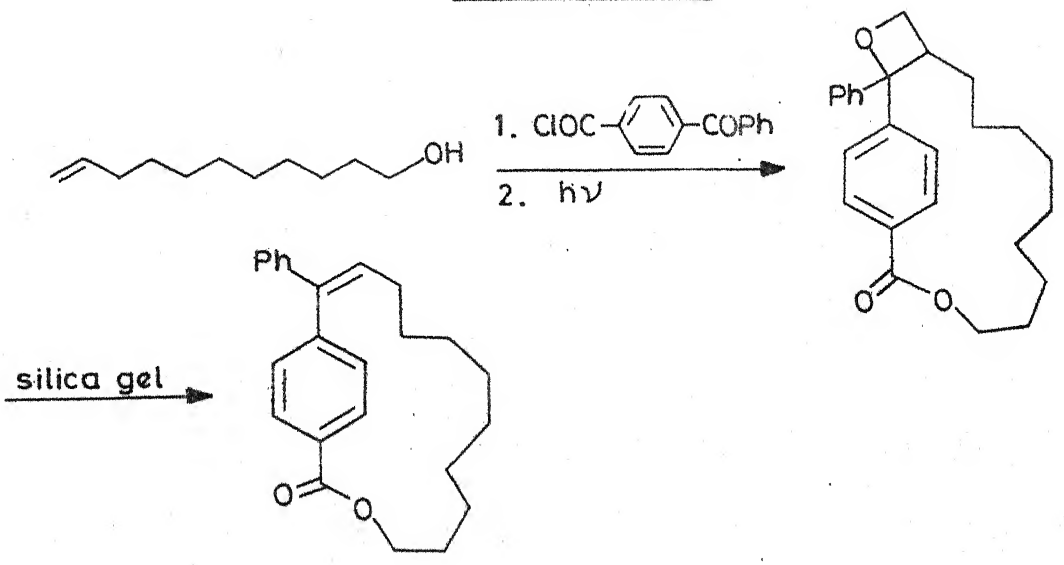


CHART B. LII

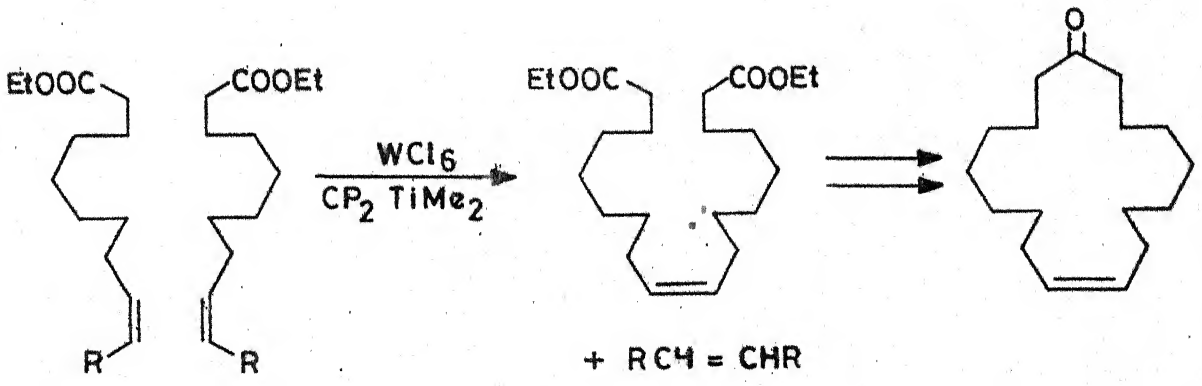
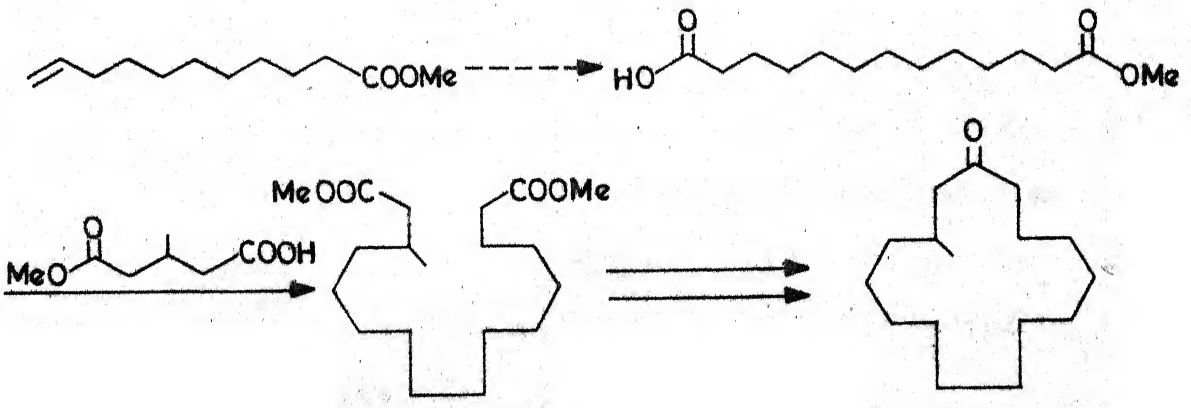


CHART B. LIII



Civetone, an important and classical ingredient in several types of perfumes, has been prepared by a particularly attractive strategy involving the metathesis of ethyl oleate followed by Dieckmann cyclisation (Chart B.LII).[53] The C-15 cyclic ketone, muscone, continues to attract synthetic interest in view of its application as a perfume. An attractive synthesis for muscone involves the electrolytic coupling of monomethyl ester of glutaric acid with methyl hydrogen tridecanoate followed by Dieckmann cyclisation (Chart B.LIII).[54]

Fatty Acids as a Source of Synthons related to Lipids

Currently, there is a great deal of interest in the straight chain C-30 alcohol, triacontanol, because of its reported ability to dramatically enhance the yields of a variety of food materials. Of the several methods that have been delineated leading to this unusual alcohol, two are particularly noteworthy. The first of these is the transformation of nonaeicosa 1-ene, prepared from a Li_2CuCl_4 mediated coupling of bromo undec 10-ene and steryl bromide, *via* peroxide mediated addition of elements of chloroform followed by hydrolysis and reduction (Chart B.LIV).[55] The second procedure is from triaconta 15-ene, arising from the metathesis of 1-hexadecene, by hydroboration, thermal boron migration to the terminus and oxidation (Chart B.LV).[56]

CHART B. LIV

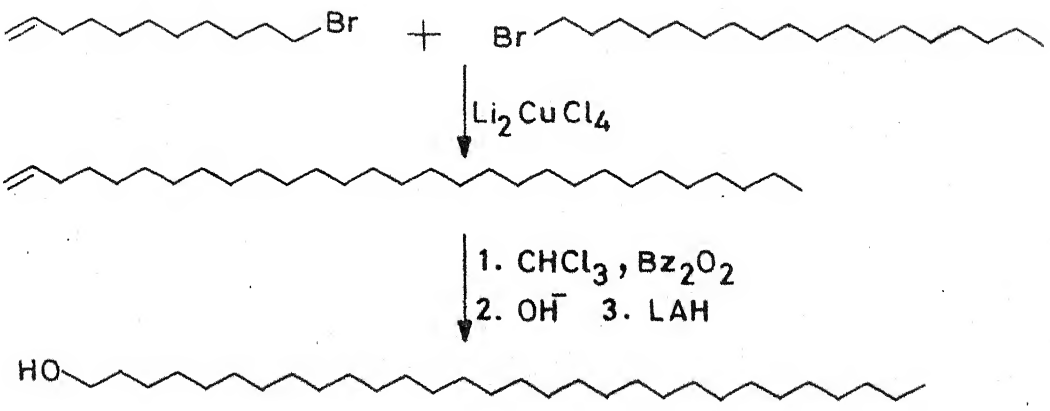


CHART B. LV

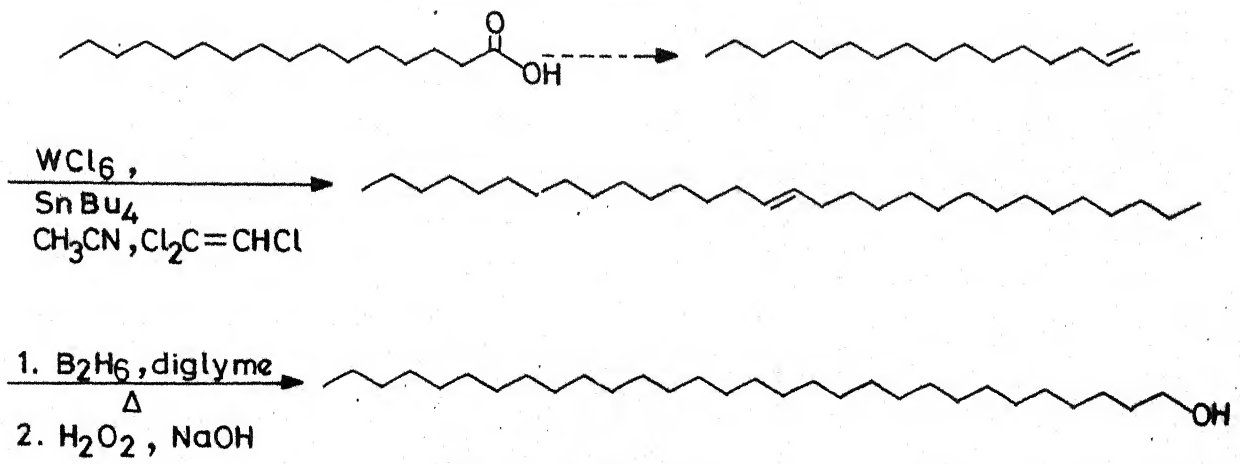
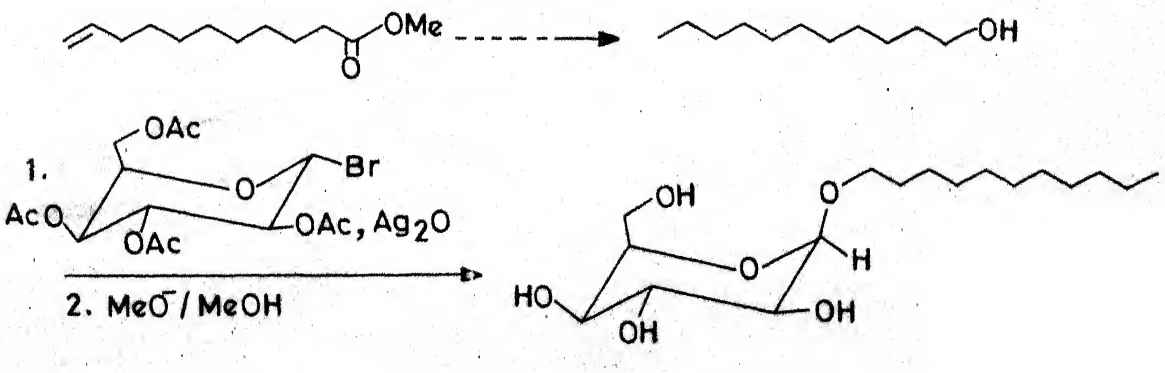


CHART B. LVI

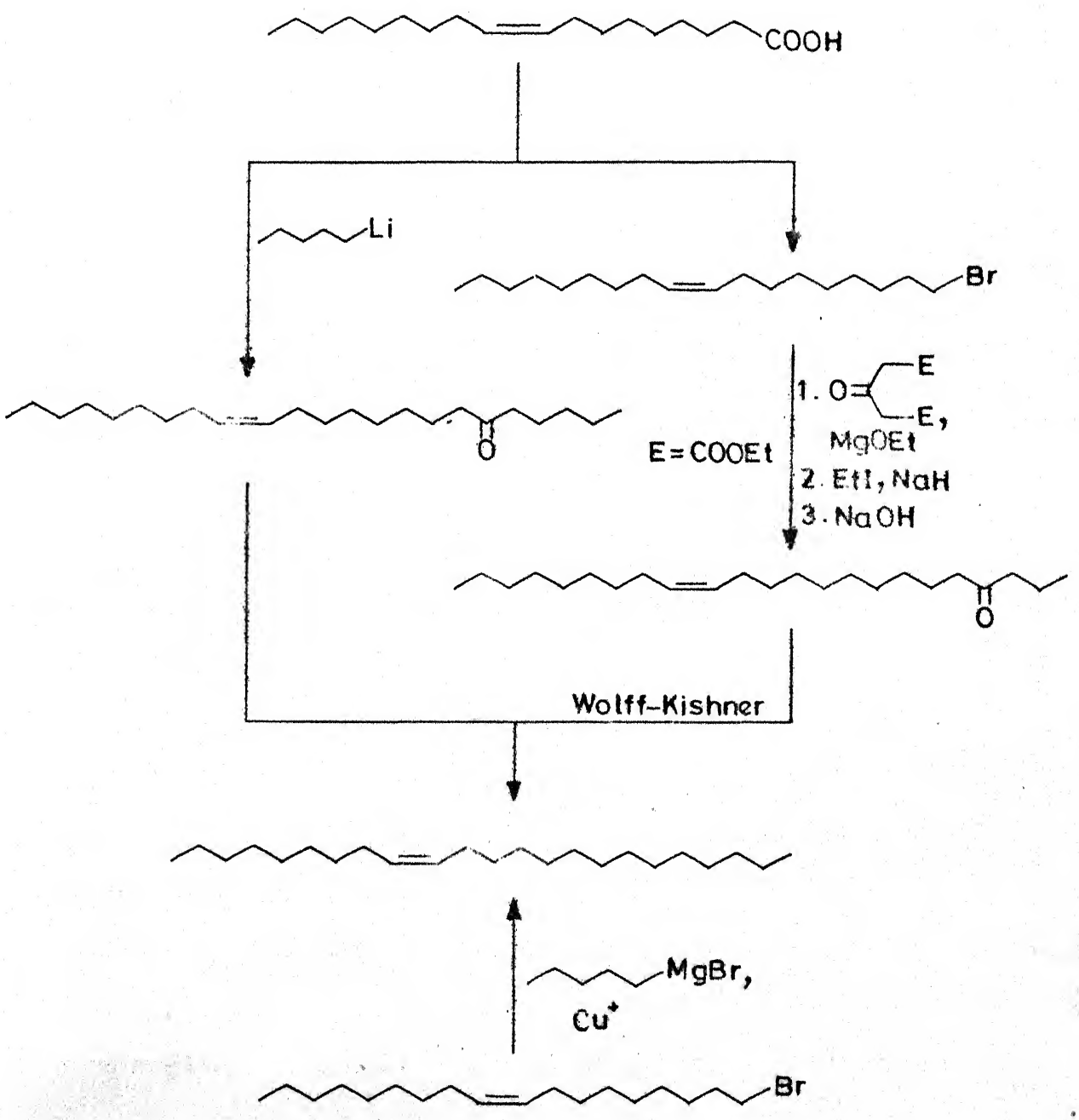


Recently, a class of lipids have been identified wherein a hydrocarbon residue is attached to sugars. The simplest of these is β-1 undecyl glucose which has been found to be particularly useful in the removal of lipids from biological samples, specially those related to visual pigments. The synthesis of this lipid is illustrated in Chart B.LVI.[57]

Fatty Acids as a Source of Synthons related to Hydrocarbons

A variety of hydrocarbons have been prepared from fatty acids *via* diverse, conventional coupling and decarboxylative procedures. The synthesis of trieicosa (Z) 9-ene, musculure, the pheromone related to the common housefly, by three different routes from oleic acid, serves as a good illustration of the continued development of methodologies relating to the transformation of fatty acids to hydrocarbons (Chart B.LVII).[58]

CHART B.LVII


COOH
Li
Br
O
E=COOEt
1. O=C(E)(E),
MgOEt
2. EtI, NaH
3. NaOH
O
Wolff-Kishner
MgBr,
Cu+
Br

C. PRESENT WORK

The central theme of the present work is the transformation of castor oil to novel acetylenic synthons and illustration of their versatility in syntheses. The choice of acetylenic precursors is related to the fact that they provide, not only a simple method for C-C bond formation but also can be transformed, with a very high degree of stereoselectivity, to Z olefins, to which category a preponderantly large number of insect sex pheromones belong. The acetylenic synthons, in turn, were prepared from methyl undec 10-enoate (2) and sebacic acid(53), both of which are the primary fragmentation products of castor oil.

1-Tetrahydropyranyloxy dodec 11-yne (8), a key synthon that has been transformed, in the present work, to several natural products, was prepared by a strategy that incorporated a terminal $\pi \longrightarrow -CH_2-C\equiv CH$ change. Another novel C-12 synthon, namely, 1-tetrahydropyranyloxy 12-hydroxy dodec 10-yne (79), was prepared by a crucial C-C bond formation with formaldehyde.

The versatility of 79 has been illustrated by its transformation to bombykol (83). The related hydroxymethyl system 84 has been transformed to traumatin (86). Non 8-ynoic acid (57), the third acetylenic synthon used in the present work, was prepared from methyl undec 10-enoate (2), as well as, from sebacic acid (53). Thus, whereas the 2 $\longrightarrow$ 57 change involved classical, repetetive degradation from the carboxyl end, the 53 $\longrightarrow$ 57 change was accomplished by a surprisingly, extraordinarily regioselective, decarboxylative π-generation, which has been demonstrated to be a general reaction for terminal $\pi \longrightarrow$ lower terminal π change, for which no clean procedures are currently available. The usefulness of 57 as an important synthon has been demonstrated with the synthesis of the sex pheromone related to the insect species Grapholita molesta (65) and the synthesis of the macrolide, recifeiolide (70).

The practical and stereochemical facets involved in the above transformations played an important role in the overall strategy. In view of the fact that insect sex pheromones are thinly spread amongst vast sexually specific insect populations, their isolation from natural sources is impractical and, therefore, any rational route to them must have practical potential. Intimately linked to this is the need for very high stereochemical purity, since, the potency of insect sex pheromones is critically linked to this criterion. The overall yield of the pheromones

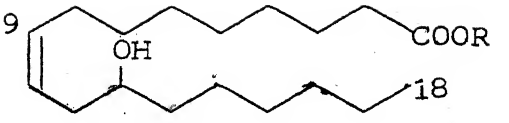
prepared in the present work was good and the stereochemical purity excellent. Representative samples of pheromones have been analysed by Dr. David R. Hall, Tropical Products Institute, London on 1.8 m x 2 mm i.d. 5% SE 30+0.5% Carbowax 20M/Chromosorb W HP, 1.8 m x 2 mm i.d. 1.5% Carbowax 20M on Chromosorb G AW DMCS, 100-120 mesh, and 1.8 m x 2 mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene on Gas Chrom Q columns.

The genesis of the work presented in this Section was, inter alia, the recognition of the striking resemblance between the C-18 castor oil (1, R=glyceride) and the C-18 insect sex pheromones of Achroia grisella (17)*,59 and Lycorea ceres ceres (19)**,60.

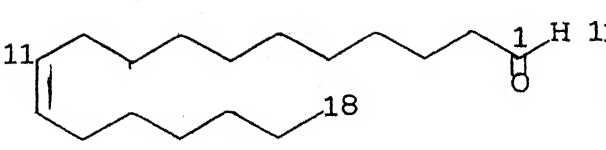
---

* Achroia grisella, a species of wax moth, are specific enemies of bees. Their caterpillars make silken tunnels in the bee-comb under cover of which they feed on bee wax. When the attack is severe, the bees are obliged to abandon their nest. The sex attractant is produced by the males in their wing glands. It consists of n-undecenal and octadec (Z) 11-en 1-al. Field trials have shown that 10 mg of undecenal and 0.1 mg of octadec (Z) 11-en 1-al can attract females.

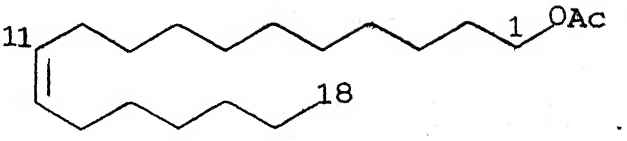
** In the Queen butterfly of the species Lycorea ceres ceres, the male members can induce a female on flight for mating by secretion of an attractant via organs called hair pencils, that can be extruded from the end of the abdomen. Solvent extraction of 100 hair pencils from live males of this species gave 8.3 mg of octadec (Z) 11-enyl acetate in addition to 2,3-dihydro 7-methyl 1H pyrrolizin 1-one (10 mg) and cetyl acetate (4.5 mg).



1



17



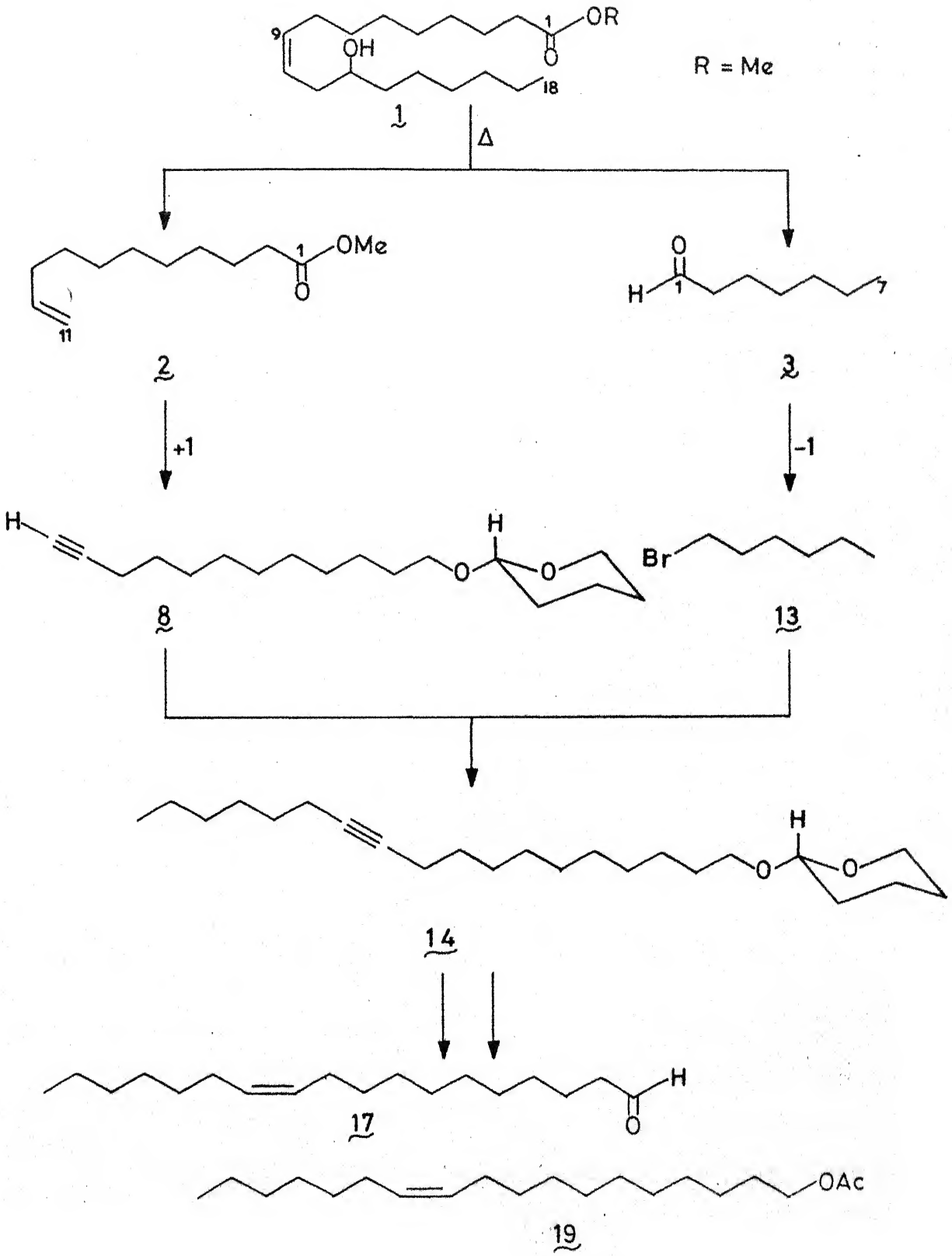
19

In the present work 1 has been re-structured to 17 and 19 from the C-11 + C-7 fragmentation products of methyl ricinoleate (1, R=Me), namely, 2 and 3, by homologation of the former to the novel key synthon, 1-tetrahydropyranyloxy dodec 11-yne (8) and the degradation of the latter to n-hexyl bromide (13) and their subsequent union (Chart C.I).

The synthesis of 1-tetrahydropyranyloxy dodec 11-yne (8) via homologation of 2

Castor oil (1, R=glyceride) was trans-esterified to methyl ricinoleate (1, R=Me), in 85% yields, with methanol containing catalytic amounts of sodium methoxide. The $\pi^2s + \sigma^2s + \sigma^2s$ fragmentation (retro-ene) of 1 (R=Me) to methyl undec 10-enoate(2) and n-heptaldehyde (3) was accomplished in 49% yields by pyrolysis over a luminous flame, the thermal distribution being effected

Chart C.I



1 → 2 (+1) and 1 → 3 (-1); 8 + 13 → 14 → 17 → 19

by support on glass-wool or sand.[61] The major fragmentation product 2 was transformed to the C-12 synthon 8, via sequence outlined in Chart C.II.a.

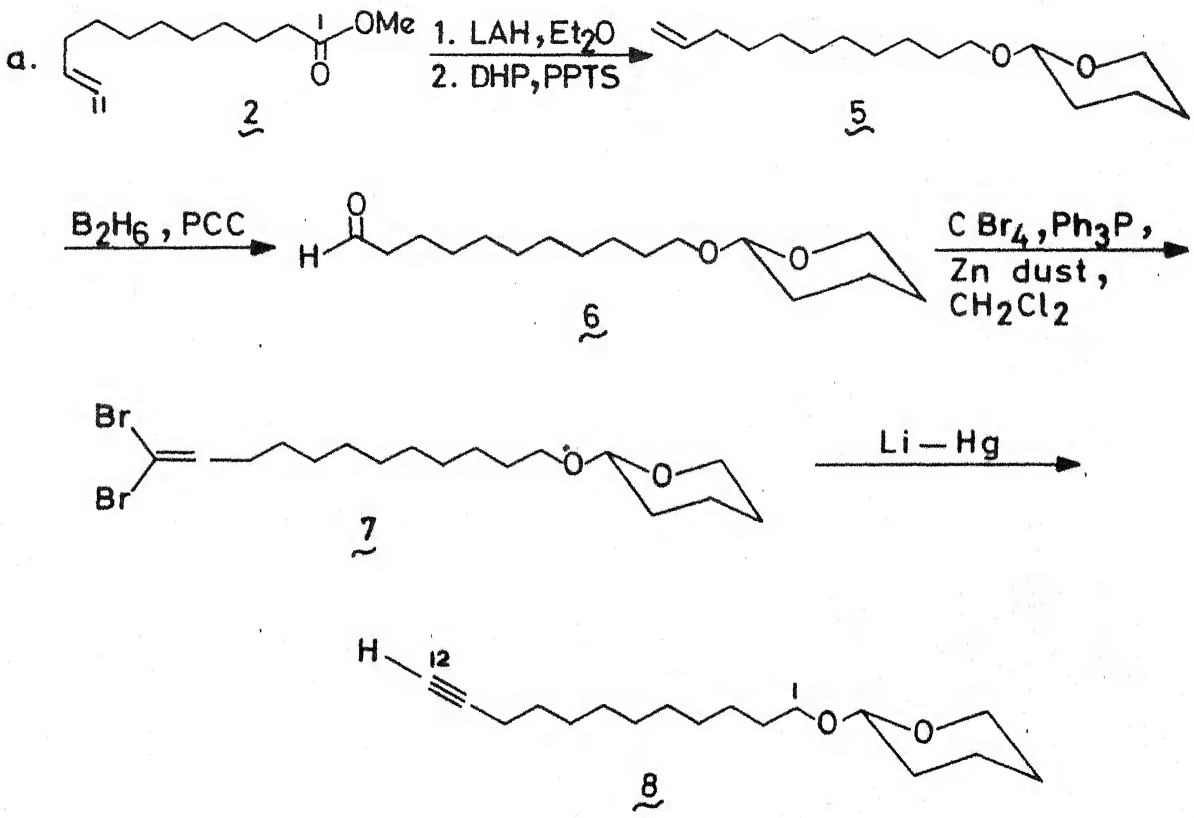
---

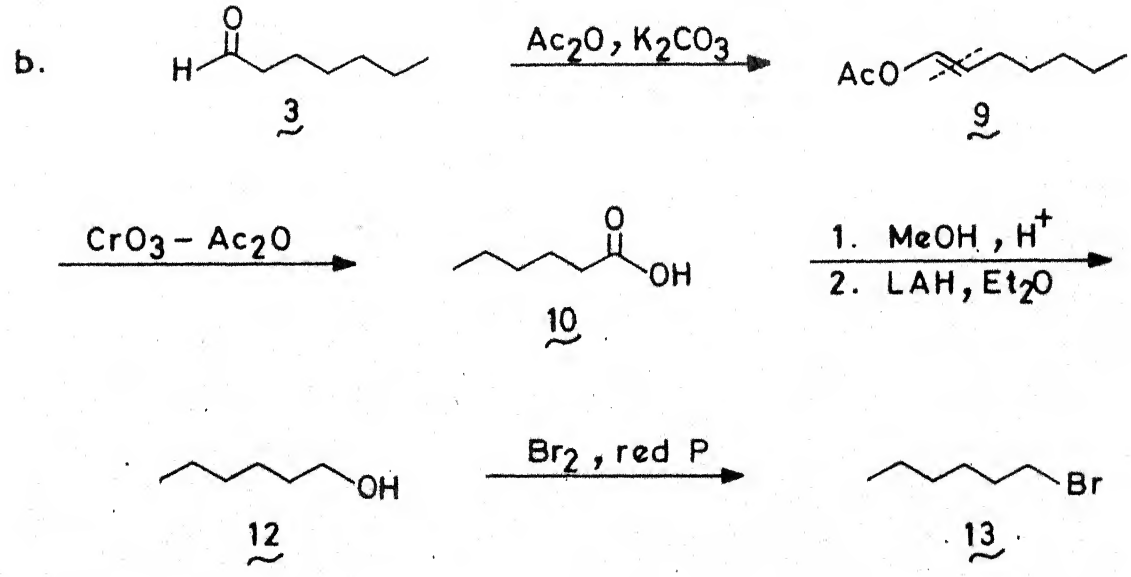
1 : bp 128-130°/0.02 torr;
ir: ν_{max}(neat)(cm^{-1}): 3440 (hydroxyl), 1742 (ester).
nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOCH_3$), 5.45 (m, 2H, $-CH=CH-$).

2 : bp 80-81°/0.09 torr;
ir: ν_{max}(neat)(cm^{-1}): 1742 (ester), 1640 (double bond).
nmr: $\delta_{(CDCl_3)}$: 3.68 (s, 3H, $-COOCH_3$), 4.98 (m, 2H, $CH_2=CH-$), 5.78 (m, 1H, $CH_2=CH-$).

Methyl undec 10-enoate (2) was transformed, in 95% yields, to 1-hydroxy undec 10-ene (4) with LAH and then to the THP ether 5 (89%) with DHP-pyridinium p-toluene sulfonate (PPTS).[62] The latter crystalline reagent makes -OH protection, as well as, -OTHP de-protection facile and clean operations, as compared to the usual PTSA, which gives dark coloured reaction mixtures. The direct transformation of 1-tetrahydropyranyloxy undec 10-ene (5) to 1-tetrahydropyranyloxy undecanal (6) was accomplished, in 72% yields, by an advantageously simplified hydroboration-oxidation sequence. The aldehyde 6 was transformed to the gem dibromo olefin 7 (79%) by in situ generated $Ph_3\overset{+}{P}-\overset{-}{C}Br_2$, from carbon-tetrabromide, and then, with 1.5% Li-Hg amalgam, conveniently prepared

Chart C.II


a.
OMe
1. LAH, Et2O
2. DHP, PPTS
2
5
B2H6, PCC
6
C Br4, Ph3P,
Zn dust,
CH2Cl2
Br
Br
7
Li—Hg
H
12
8


b.
3
Ac2O, K2CO3
AcO
9
CrO3 – Ac2O
10
OH
1. MeOH, H+
2. LAH, Et2O
12
OH
Br2, red P
13
Br

under hot tetralin, to the acetylene 8 (47%; overall yield from 2, 23%) (Chart C.II.a). The yield in the 7 ⟶ 8 change reflects the fact that the precursors 6 and 7 were used without further purification because of their limited stability.

---

4 : bp 76-80°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 1645 (double bond).

5 : bp 85-88°/0.05 torr;

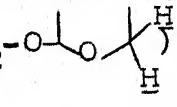
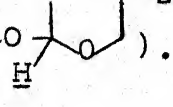
ir: ν_{max}(neat)(cm^{-1}): 1640 (double bond), 1135, 1120, 1080, 1030 (-OTHP).

6 : ir: ν_{max}(neat)(cm^{-1}): 1730 (aldehyde), 1135, 1120, 1080, 1030 (-OTHP).

7 : ir: ν_{max}(neat)(cm^{-1}): 1620 (double bond), 1135, 1120, 1080, 1030 (-OTHP).

8 : bp 120-123°/0.2 torr;

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.9 (t, 1H, H-C≡C-), 2.25 (m, 2H, -C≡C-CH_2-), 3.2-4.0 (m, 4H, -CH_2-O- ), 4.58 (s, 1H, -O- ).

The degradation of heptaldehyde (3) to n-hexyl bromide (13)

The transformation of the minor fragment, n-heptaldehyde(3), to n-hexyl bromide (13) was accomplished in 38% overall yield via sequence outlined in Chart C.II.b. Freshly distilled 3 was transformed, with freshly ignited K_2CO_3 and acetic anhydride, to 1-acetoxy heptene (9) (76%). The latter was degraded, with CrO_3-Ac_2O, to hexanoic acid (10) (66%). Fischer esterification with MeOH-H_2SO_4 gave methyl hexanoate (11) (100%) which was transformed, with LAH, to n-hexanol (12) (92%), and then with red phosphorus- bromine to n-hexyl bromide (13) (81%) whose ir was identical with that of an authentic sample.

---

9 : bp 88-90°/17 torr;

ir: ν_{max}(neat)(cm^{-1}): 1760 (acetate), 1675 (double bond).

10: bp 45-46°/0.9 torr;

ir: ν_{max}(neat)(cm^{-1}): 1710 (carboxylic acid).

11: bp 150°/760 torr;

ir: ν_{max}(neat)(cm^{-1}): 1742 (ester).

12: bp 155-156°/760 torr;

ir: ν_{max}(neat)(cm^{-1}): 3360 (hydroxyl).

The synthesis of 1-oxo octadec (Z) 11-ene (17), the sex pheromone of Achroia grisella and 1-acetoxy octadec (Z) 11-ene (19), the sex pheromone of Lycorea ceres ceres

The re-structured fragments 8 and 13 were united via acetylide, in HMPT, leading to 1-tetrahydropyranyloxy octadec 11-yne (14) (94%). De-protection of 14 with PPTS-EtOH to 15(100%) followed by stereoselective reduction, in 96% yield, using 5% $Pd/BaSO_4$, further deactivated with a micro-drop of synthetic quinoline, and PCC oxidation of the resulting 16 gave 1-oxo octadec (Z) 11-ene (17) (97%), the sex pheromone related to the insect species Achroia grisella (overall yield from 14, 93%). Alternately, direct -OTHP $\longrightarrow$ -OAc transformation of 14 with AcOH:AcCl::10:1 to 18, in 88% yield, followed by stereoselective hydrogenation gave 1-acetoxy octadec (Z) 11-ene (19) (97%), the sex pheromone related to the species Lycorea ceres ceres, in an overall yield of 85.2% from 14 (Chart C.III).

---

14 : bp 140-145°/0.03 torr;

ir: ν_{max}(neat) (cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

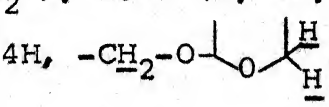
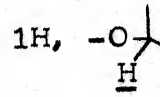
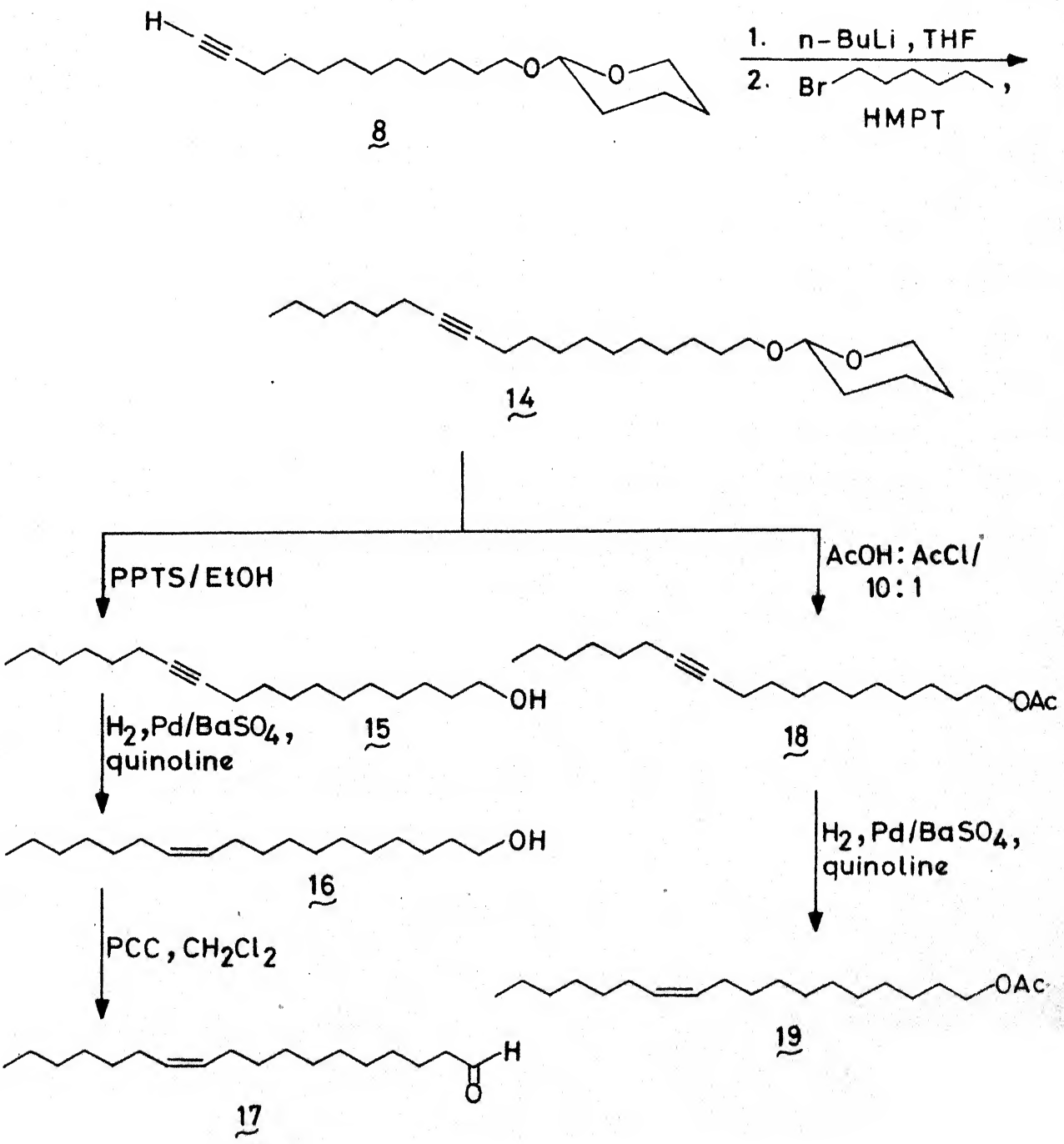
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, CH_3-CH_2-), 2.05 (m, 4H, $-CH_2-C\equiv C-CH_2-$), 3.15-4.0 (m, 4H, $-CH_2-O-$ ), 4.5 (s, 1H, ).

Chart C.III


H
O
O
8
1. n-BuLi, THF
2. Br
HMPT
14
PPTS/EtOH
AcOH: AcCl/
10:1
OH
15
OAc
18
H2, Pd/BaSO4,
quinoline
16
H2, Pd/BaSO4,
quinoline
PCC, CH2Cl2
19
17

15 : bp 103-107°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 3330 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 2.1 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 3.08 (s, 1H, $-CH_2-O\underline{H}$), 3.5 (t, 2H, $-C\underline{H}_2-OH$).

16 : bp 105°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 3330 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.5 (t, 3H, $-C\underline{H}_2-O\underline{H}$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

17 : ir: ν_{max}(neat)(cm^{-1}): 1730 (aldehyde).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.98 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 2.32 (t, 2H, $-C\underline{H}_2-CHO$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$), 9.65 (t, 1H, $-C\underline{H}O$).

18 : bp 106-110°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (s, 3H, $-OCOC\underline{H}_3$), 2.05 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 3.98 (t, 2H, $-C\underline{H}_2-OCOCH_3$).

19 : ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.8 (t, 3H, $C\underline{H}_3-CH_2-$), 1.9 (s, 3H, $-OCOC\underline{H}_3$), 3.93 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

GC analyses of 19, by Dr. David R. Hall, Tropical Research Institute, England, on 6'x 2mm i.d. 5% SE 30/0.5% Carbowax 20M

on Chromosorb W HP and 6'x 2mm i.d. 1.5% Carbowax 20M/Chromosorb G AW DMCS columns showed that the gross impurity present (< 5%) was 8. Analysis on a special 1.8m x 2mm i.d. 5% 4-(p-methoxy-cinnamyloxy)-4'-methoxyazobenzene column showed that the stereochemical purity was 98.3% the desired Z isomer.

To the best of our knowledge, the present work reports the first synthesis of the pheromone of the species, Achroia grisella (17). In terms of the availability of starting materials, yields and stereochemical purity the procedures presented here should be the most attractive for the pheromones related to A. grisella and L. ceres ceres.

A very large number of insect sex pheromones possess the general structure R-CH=CH-$(CH_2)_n$-CHXY which, antithetically, could be analysed in terms of the union of the hydrophobic R segment with the functional group carrying methylene chain. 1-Tetrahydropyranyloxy dodec 11-yne (8), therefore, should be an excellent synthon for insect sex pheromones of the category R-CH=CH-$(CH_2)_9$-CHXY wherein the π stereochemistry can be generated as desired. This has been illustrated in the present work.

The synthesis of 1-hydroxy hexadec (Z) 11-ene (22), the sex pheromone of Mamestra configurata*,[63] and 1-acetoxy hexadec (Z) 11-ene (24), the sex pheromone of Scotogramma trifolii**,[64]

1-Tetrahydropyranyloxy dodec 11-yne (8) was transformed, via alkylation of the lithium acetylide with 2 equivalents of n-butyl bromide in HMPT, to 1-tetrahydropyranyloxy hexadec 11-yne (20) (96%). De-protection of 20 with PPTS-EtOH gave the alcohol 21 in 98% yields which was stereoselectively hydrogenated to 1-hydroxy hexadec (Z) 11-ene (22) (93%), the sex pheromone of

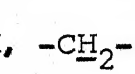
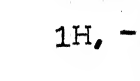
---

* A potent sex pheromone, Z 11-hexadecen 1-ol, was isolated from female Mamestra configurata, the bertha armyworm moth. Maximum biological response in laboratory bioassays with synthetic compounds was obtained with a mixture of 85% Z and 15% E isomers.

** Two major components of the sex pheromone of Scotogramma trifolii, clover cutworm moth, were isolated from extracts of female abdominal tips and identified as hexadec (Z) 11-en 1-ol and its acetate. Both (Z) 11-hexadecenyl alcohol and (Z) 11-hexadecenyl acetate were obligatory for effective field trapping of male moths. Alcohol to acetate ratios between 1:1 and 1:9 gave good capture rates, the higher ratios were somewhat more effective than the lower ones.

Mamestra configurata (overall yield from 8, 86.9%). Direct transformation of 20 to 1-acetoxy hexadec 11-yne (23) in 83% yields, with AcOH:AcCl::10:1,followed by stereoselective hydrogenation gave 24 (97%), the sex pheromone of Scotogramma trifolii (overall yield from 8, 76.8%) (Chart C.IV). The stereochemical purity of the acetate 24 was inferred to be ~95% of the desired Z isomer based on the GC analysis of its lower homolog on a liquid crystal column. The same order of purity can, therefore, be anticipated for the alcohol 22. The procedures described in the present work should be the most attractive for the preparation of pheromones 22 and 24.

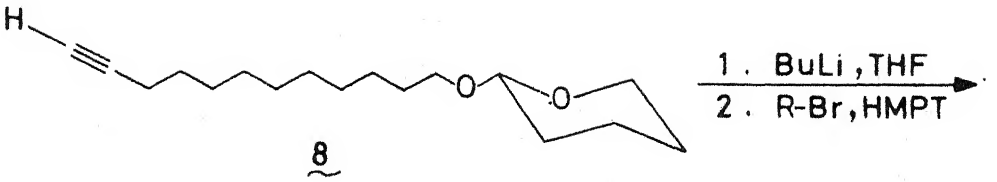
---

20 : ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 2.05 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 3.0-4.0 (m, 4H, $-C\underline{H}_2-O$ ), 4.5 (s, 1H, ).

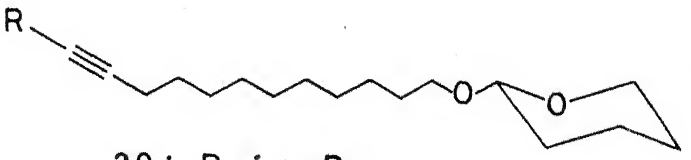
21 : bp 95°/0.03 torr;
ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 2.05 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 2.4 (s, 1H, $-CH_2-O\underline{H}$), 3.5 (t, 2H, $-C\underline{H}_2-OH$).

22 : ir: ν_{max}(neat)(cm^{-1}): 3320 (hydroxyl).
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 2.8 (s, 1H, $-CH_2-O\underline{H}$), 3.5 (t, 2H, $-C\underline{H}_2-OH$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

Chart C.IV



8

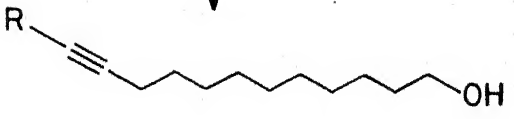


20 : R = n-Bu

25 : R = Et

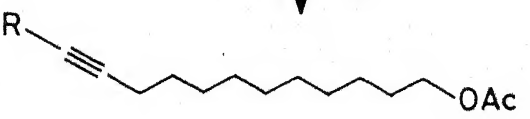
PPTS/EtOH

AcOH : AcCl
10 : 1



21 : R = n-Bu

26 : R = Et

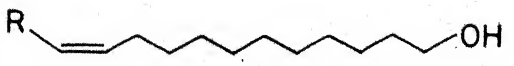


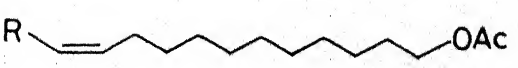
23 : R = n-Bu

28 : R = Et

H_2, Pd/$BaSO_4$, quinoline

H_2, Pd/$BaSO_4$, quinoline





22 : R = n-Bu

27 : R = Et

24 : R = n-Bu

29 : R = Et

23: bp 90°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 7H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.98 (t, 2H, $-C\underline{H}_2-OCOCH_3$).

24 : ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 7H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.95 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

The synthesis of 1-hydroxy tetradec (Z) 11-ene (27), the sex pheromone of Archips rosanus*,[65] and 1-acetoxy tetradec (Z) 11-ene (29), the sex pheromone of Choristoneura rosaceana*,[66]

In the present work, the synthesis of the pheromones of

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* Archips rosanus, European leaf roller moth, and Choristoneura rosaceana, oblique banded leaf roller moth, are species of insects with highly specialized capacity to roll leaves in precise geometrical patterns after destroying the leaf by cutting the veins, stalk and leaves. The major objective of this astonishing exercise is to deposit eggs. Two pheromone components, Z 11-tetradecenyl acetate and Z 11-tetradecen 1-ol in the ratio 9:1 were identified in the female abdominal tips of Archips rosanus. Neither compound alone was attractive to the male of the species. In field trials, in apple orchards, as little as 0.01 mg of tetradec (Z) 11-enyl acetate, the sex pheromone of Choristoneura rosaceana, was effective in attracting males of the species. Traps baited with the synthetic pheromone caught numerous males in field tests.

the insect species Archips rosanus, and Choristoneura rosaceana, was achieved from 1-tetrahydropyranyloxy dodec 11-yne (8). The lithium acetylide from 8 was alkylated with bromoethane in HMPT to give 1-tetrahydropyranyloxy tetradec 11-yne (25) (93%). De-protection of 25 with PPTS-EtOH gave 1-hydroxy tetradec 11-yne (26) (91%). The latter, on stereoselective hydrogenation, gave 1-hydroxy tetradec (Z) 11-ene (27) (97%), the sex pheromone of A. rosanus in an overall yield of 82.2% from 8. Alternately, 25 was directly transformed, with AcOH:AcCl::10:1, to 1-acetoxy tetradec 11-yne (28) (91%) which, on stereoselective hydrogenation, gave, in 98% yields, the pheromone of C. rosaceana, 1-acetoxy tetradec (Z) 11-ene (29) (Chart C.IV) (overall yield from 8, 83%).

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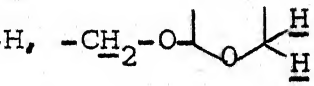
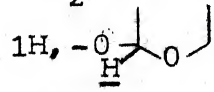
25 : bp 125-130°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $\underline{CH_3}-CH_2-$), 2.05 (m, 4H, $-\underline{CH_2}-C\equiv C-\underline{CH_2}-$), 3.1-4.0 (m, 4H, $-\underline{CH_2}-O-$ ), 4.4 (s, 1H, ).

26 : bp 90°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $\underline{CH_3}-CH_2-$), 2.1 (m, 4H, $-\underline{CH_2}-C\equiv C-\underline{CH_2}-$), 2.95 (s, 1H, $-CH_2-\underline{OH}$), 3.52 (t, 2H, $-\underline{CH_2}-OH$).

27 : ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$:0.95(t,3H,$\underline{CH_3}$-CH_2-), 1.95 (m, 4H,-$\underline{CH_2}$-CH=CH-$\underline{CH_2}$-), 3.5 (t, 3H, -$\underline{CH_2}$-$\underline{OH}$), 5.2 (m, 2H, -$\underline{CH}$=$\underline{CH}$-).

28 : bp 112-115°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $\underline{CH_3}$-CH_2-), 1.8 (s, 3H, -OCO$\underline{CH_3}$), 2.1 (m, 4H, -$\underline{CH_2}$-C≡C-$\underline{CH_2}$-), 3.9 (t, 2H, -$\underline{CH_2}$-OCOCH_3).

29 : ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $\underline{CH_3}$-CH_2-), 2.05 (m, 7H, -OCO$\underline{CH_3}$, -$\underline{CH_2}$-CH=CH-$\underline{CH_2}$-), 3.95 (t, 2H, -$\underline{CH_2}$-OCOCH_3), 5.28 (m, 2H, -$\underline{CH}$=$\underline{CH}$-).

GC analysis of 29, on a 1.8m x 2mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene on Gas Chrom Q column, showed that it contained, at least, 95% of the desired Z isomer. The same order of selectivity can be inferred for the alcohol 27. The procedures developed in the present work offer effective and practical routes to the pheromones 27 and 29.

The pheromones described above have the Z configuration. The synthon 8, from which these were prepared, is equally versatile for the preparation of pheromones having E configuration. This is illustrated with the synthesis of pheromones related to Archips argyrospylus and Platyonota stultana.

The synthesis of 1-hydroxy tetradec (E) 11-ene (31), the sex pheromone of Archips argyrospylus*,67 and 1-acetoxy tetradec (E) 11-ene (32), the sex pheromone of Platyonota stultana**,68

The synthesis of the pheromones 31 and 32 was achieved in the present work via 1-tetrahydropyranyloxy tetradec 11-yne (25). Sodium-liquid ammonia reduction of 25 gave 1-tetrahydropyranyloxy tetradec (E) 11-ene (30) in 89% yield. De-protection of 30 with PPTS-EtOH gave 1-hydroxy tetradec (E) 11-ene (31) (90%), the sex pheromone of Archips argyrospylus. Direct -OTHP ⟶ -OAc change, effected by AcOH:AcCl::10:1, led to 1-acetoxy tetradec (E) 11-ene (32) (87%), the sex pheromone of Platyonota stultana (Chart C.V).

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* Female abdominal tip extracts of Archips argyrospylus, fruit tree leaf roller moth, contain dodecyl acetate, Z and E 11-tetradecen 1-ols (60:40) and Z and E 11-tetradecenyl acetates.

** A mixture of E and Z 11-tetradecenyl acetates was found in the omnivorous leaf roller moth, Platyonota stultana, female tip extracts in a ratio of 88:12 respectively. In the field, they were most attractive to male moths of the species, in a ratio of E:Z::94:6. Field attractivity was increased by addition of small quantities (0.2-2.0%) of mixtures of E and Z 11-tetradecenyl alcohols, which were present in the female tip extracts in a ratio of 88:12 respectively.
1-Acetoxy tetradec (E) 11-ene has also been identified as a pheromone component of the insect species, Argyrotaenia velutinana (red banded leaf roller moth); Spodoptera littoralis (Egyptian cotton leafworm moth) and Archips podana (fruit tree tortrix moth).

Chart C.V

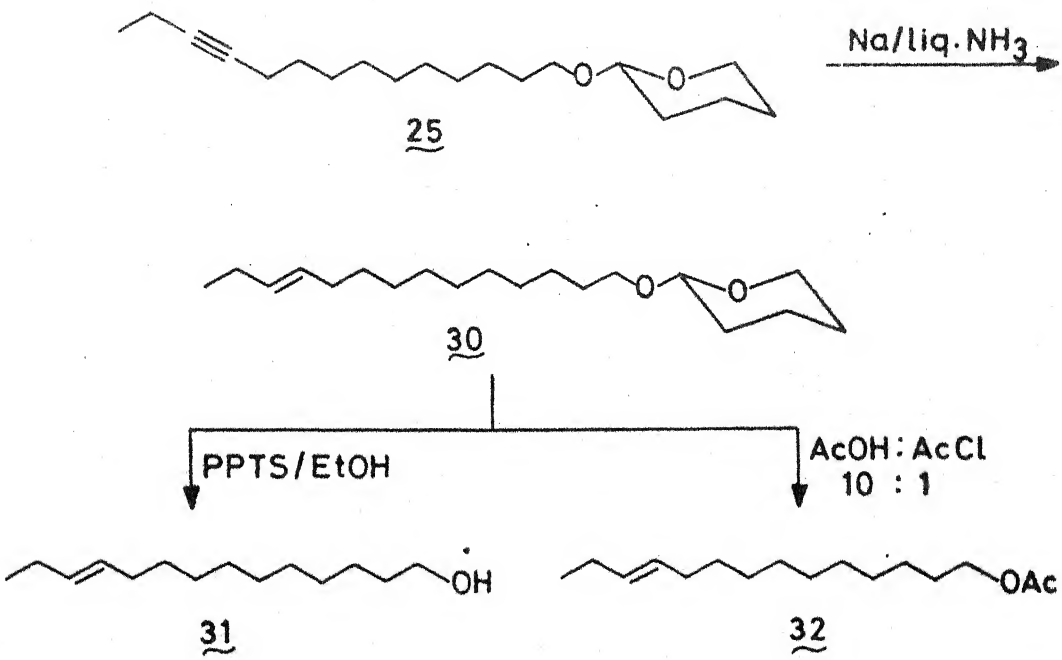
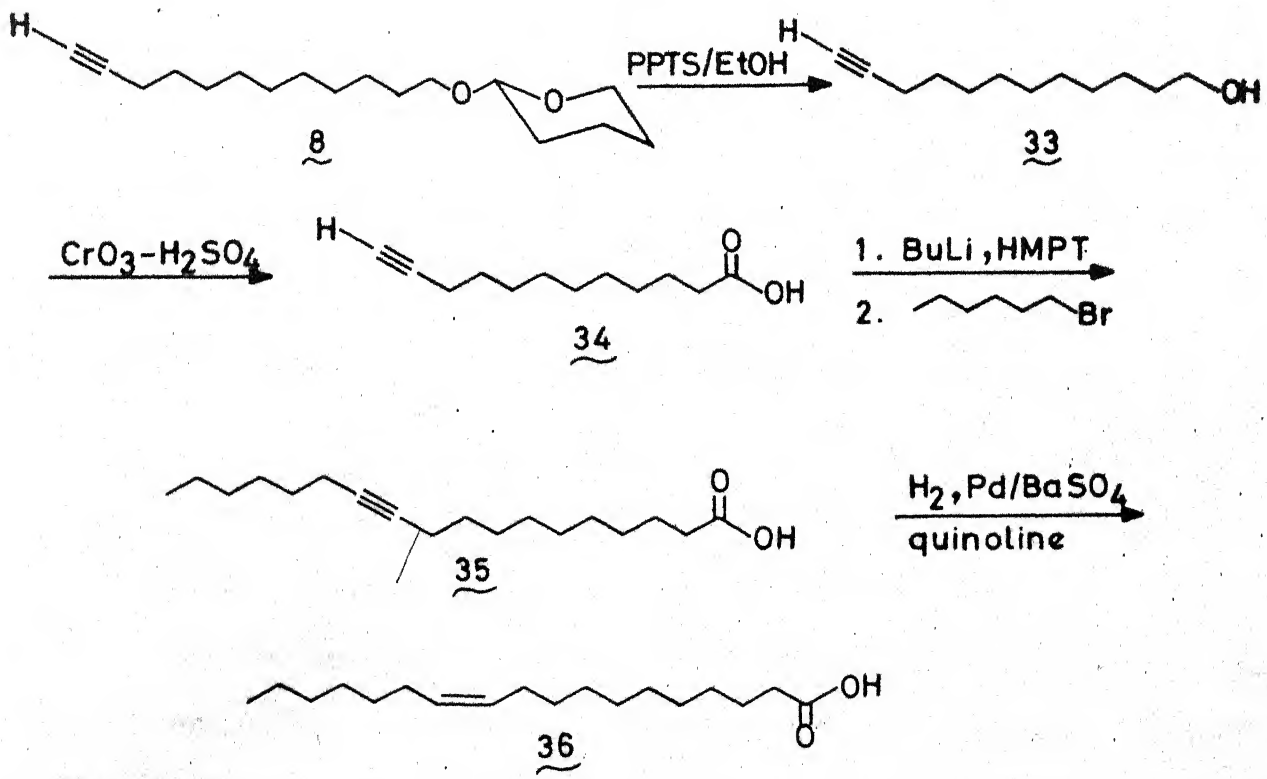


Chart C.VI



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30 : ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.0-4.0 (m, 4H, $-C\underline{H}_2-O$-THP), 4.5 (s, 1H, $-O\underline{H}$-THP), 5.32 (m, 2H, $-C\underline{H}=C\underline{H}-$).

31 : ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.5 (m, 3H, $-C\underline{H}_2-O\underline{H}$), 5.32 (m, 2H, $-C\underline{H}=C\underline{H}-$).

32 : ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 7H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.98 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.32 (m, 2H, $-C\underline{H}=C\underline{H}-$).

There exists a remarkable similarity between insect sex pheromones and fatty acids. Specific examples of this have been cited earlier in this Section. In several cases, both fatty acids and insect sex pheromones have a similar carbon backbone and their syntheses could be antithetically analysed in terms of a polar head segment and a hydrophobic tail moiety. The latter, consisting essentially of methylene chains, is shorter in insect sex pheromones as compared to fatty acids. With reference to the polar head segment, whilst the chain length is similar, the head groups in insect sex pheromones consist of, relatively, less polar

functional groups, such as, -OH, -OAc, -CHO and -COOEt, compared to the fatty acids where the end group, naturally, is a carboxyl function. Therefore, synthons related to insect sex pheromones can also be effectively used for the preparation of rare fatty acids. Thus, 1-tetrahydropyranyloxy dodec 11-yne (8) could be a precursor to fatty acids of the type, R-CH=CH-$(CH_2)_9$-COOH, such as vaccenic acid (R= $-C_6H_{13}$), lesquerolic acid (R=C_6H_{13}-CH(OH)-CH_2-) and mycolic acid (R= $-C_6H_{13}$; -CH=CH- = cyclopropane). This conclusion has been successfully tested with the synthesis of vaccenic acid (36) in the present work.

The preparation of octadec (Z) 11-enoic acid (36, vaccenic acid) via the key synthon dodec 11-ynoic acid (34)

A practical and convenient route to the naturally occurring rare fatty acid, octadec (Z) 11-enoic acid (36, vaccenic acid) from the synthon 8 has been demonstrated in the present work. De-protection of 1-tetrahydropyranyloxy dodec 11-yne (8) with PPTS-EtOH gave 1-hydroxy dodec 11-yne (33) (98%), which was transformed to the key synthon dodec 11-ynoic acid (34) (86%) by Jones' oxidation. C-Alkylation of the dilithium salt of 34 with n-hexyl bromide (13) in HMPT led to octadec 11-ynoic acid (35) (84%) which was stereoselectively hydrogenated to Z-vaccenic acid (36) (93%) (Chart C.VI).

---

33 : ir: ν_{max}(neat) (cm^{-1}): 3340 (hydroxyl), 3310 (-C≡C-H), 2120 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.79 (t, 1H, H-C≡C-), 2.05 (m, 2H, H-C≡C-CH_2-), 2.83 (s, 1H, -CH_2-OH), 3.4 (t, 2H, -CH_2-OH).

34 : ir: ν_{max}(neat) (cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1710 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 1.69 (t, 1H, H-C≡C-), 2.1 (m, 4H, H-C≡C-CH_2-, -CH_2-COOH), 11.2 (s, 1H, -COOH).

35 : ir: ν_{max}(neat) (cm^{-1}): 1710 (carboxylic acid).

36 : ir: ν_{max}(neat) (cm^{-1}): 1710 (carboxylic acid).

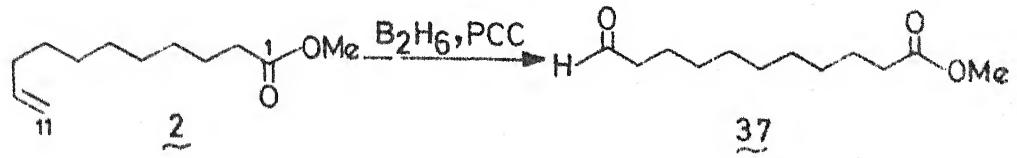
nmr: $\delta_{(CCl_4)}$: 1.82 (t, 3H, CH_3-CH_2-), 1.9 (m, 4H, -CH_2-CH=CH-CH_2-), 2.2 (t, 2H, -CH_2COOH), 5.19 (m, 2H, -CH=CH-).

It should be noted that the synthesis of vaccenic acid(36) was done with 1-tetrahydropyranyloxy dodec 11-yne (8). In principle, dodec 11-ynoic acid (34) or its derivatives, should be a better choice compared to 8 since this would enable the retention of the carboxyl function from methyl undec 10-enoate to the products. In the event, however, the transformation of methyl undec 10-enoate (2) to methyl dodec 11-ynoate (40) by pathways similar to that involved in the 6 ⟶ 8 change was

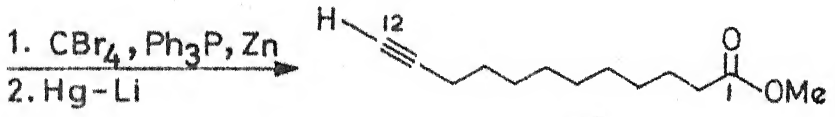
beset with difficulties arising from the susceptibility of the ester function to undergo reduction by diborane. This was inferred from the fact that the sequence of reactions gave rise to two acetylenic products. GC on 3% SE-30 column showed that their composition was nearly 1:1. Careful chromatographic separation led to the identification of these as the desired methyl dodec 11-ynoate (40) and trideca 1,12-diyne (41). The formation of 41 was rationalized on the basis of the concomitant diborane reduction of the ester function in 2 leading to undecane 1,11-diol, which underwent PCC oxidation to the dialdehyde 38, and then, gave the diacetylene 41 under conditions of the 6 → 8 change (Chart C.VII.a; Chart C.VII.b). Indeed, it was found that this observation could be exploited for a practical route to the C-13 1,12-diacetylene 41 by treatment of 2 with excess nascent diborane followed by further operations. Subsequent experiments have shown that the selective hydroboration of the terminal system in methyl undec 10-enoate (2) can be achieved by controlling the amount of diborane and recovery of unchanged 2 (vide infra). From this it was inferred that the reaction of diborane with the terminal π system takes place in preference to the reduction of the ester grouping and such a rationalization led to the choice of a t-butyl ester, wherein it was anticipated that the diborane attack would be minimal. This expectation was fully realized.

Chart C.VII

a.

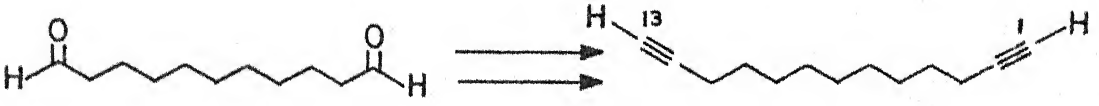


2 37



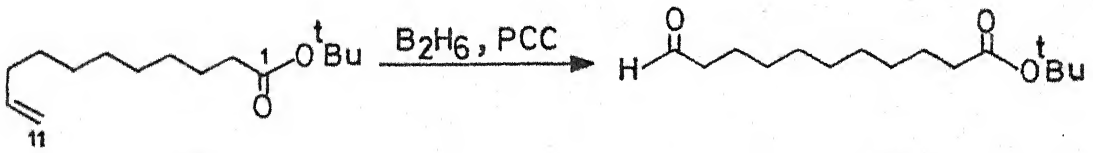
40

b.

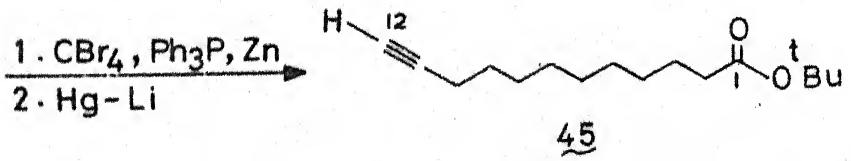


38 41

Chart C.VIII



42 43



45

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37 : ir: ν_{max}(neat)(cm^{-1}): 1735 (ester), 1720 (aldehyde).

39 : ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1620 (double bond).

40 : bp 50-52°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1740(ester).

nmr: $\delta_{(CCl_4)}$: 1.95 (t, 1H, H-C≡C-), 2.35 (m, 4H, H-C≡C-CH_2-, -CH_2-COOMe), 3.72 (s, 3H, -COOCH_3).

41 : ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-).

nmr: $\delta_{(CDCl_3)}$: 1.68 (t, 2H, H-C≡C-), 2.05 (m, 4H, H-C≡C-CH_2-).

The synthesis of t-butyl dodec 11-ynoate (45)

t-Butyl undec 10-enoate (42) was prepared in 63% yield by treatment of undecenoic acid - obtained by saponification of 2 - with isobutylene and H_2SO_4 (catalyst) in a pressure vessel. The transformation of 42 to t-butyl dodec 11-ynoate (45) was accomplished with an overall yield of 23% via procedures described above (Chart C.VIII). Thus, although the -CH=CH_2 ⟶ -CH_2-C≡CH change could be carried out retaining the ester function with yields comparable to the 2 ⟶ 8 change, preliminary experiments to transform 45 to the corresponding acid, a pre-requisite for acetylide alkylation did not yield satisfactory results. Consequently, within the framework of the present work, the synthon 8

should be considered as the best precursor for fatty acids as well.

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42 : ir: ν_{max}(neat)(cm^{-1}): 1730 (ester), 1635 (double bond).
nmr: $\delta_{(CCl_4)}$: 1.4 (s, 9H, $-COOC(\underline{CH_3})_3$), 2.05 (m, 4H, $H_2C=CH-\underline{CH_2}-$, $-\underline{CH_2}-COO^tBu$), 4.85 (m, 2H, $\underline{H_2}C=CH-$), 5.75 (m, 1H, $H_2C=\underline{CH}-$).

43 : ir: ν_{max}(neat)(cm^{-1}): 1730 (broad, aldehyde, ester).

44 : ir: ν_{max}(neat)(cm^{-1}): 1730 (ester), 1620 (double bond).

45 : ir: ν_{max}(neat)(cm^{-1}): 3310 ($-C\equiv C-H$), 2120 ($-C\equiv C-$), 1730 (ester).
nmr: $\delta_{(CCl_4)}$: 1.4 (s, 9H, $-COOC(\underline{CH_3})_3$), 1.78 (t, 1H, $\underline{H}-C\equiv C-$), 2.1 (m, 4H, $H-C\equiv C-\underline{CH_2}-$, $-\underline{CH_2}-COO^tBu$).

Attempted one carbon homologation of methyl undec 10-enoate (2) to methyl dodec 11-ynoate (40) by addition of $\pm CBr_2$ followed by cyclopropylidine collapse did not succeed due to the failure to bring about the carbene addition.

The synthons thus far described in the present work and those made earlier in our group[61,69] are related to the $\pi^2s + \sigma^2s + \sigma^2s$ transformation product of castor oil, namely, methyl undec 10-enoate (2). Indeed, nearly all the synthons

derived from castor oil which have found application in the synthesis of a variety of products are derived from 2. This is reflected from the account given in Section B. In contrast, sebacic acid (53), the product from alkaline degradation of castor oil, has received scant attention as a source of synthons. In our continuing programme directed at the exploration of castor oil as a source of synthons, it was considered interesting to examine the possibilities for re-structuring sebacic acid (53) to synthons related to the present work. The natural choice was non 8-ynoic acid (57). Not only could 57 be related to pheromones of the type $R-CH=CH-(CH_2)_6-CH_2X$, but also, it could logically find a place in the series of acetylenic synthons thus far generated from castor oil, namely, 1-tetrahydropyranyloxy dodec 11-yne (8), 1-tetrahydropyranyloxy undec 10-yne (78), and 1-tetrahydropyranyloxy dec 9-yne.[69] The transformation of sebacic acid (53) to non 8-ynoic acid (57) has been accomplished by a procedure that involves a surprisingly, extraordinarily regioselective π-generation.

The preparation of non 8-ynoic acid (57)

Sebacic acid (53) was transformed, with MeOH - H_2SO_4 (catalyst), to dimethyl decane 1,10-dioate (54) (91%). Carefully controlled partial hydrolysis of the diester 54 with barium hydroxide octahydrate in methanol-benzene, followed by isolation

and acidification of the resulting crystalline barium salt gave methyl decane 1,10-dioic acid monoester (55) (81%).[70] Oxidative decarboxylation of 55 with freshly prepared lead tetraacetate[71] gave, cleanly, methyl non 8-enoate (56) (45%) with no detectable amount of the internal olefin (NMR). Addition of bromine to 56 gave methyl 8,9-dibromo nonanoate (100%) which, under very carefully controlled treatment with aqueous KOH (135-145°C, 4 hr), gave non 8-ynoic acid (57) in 88% yield (Chart C.X) (overall yield from sebacic acid, 33.2%).

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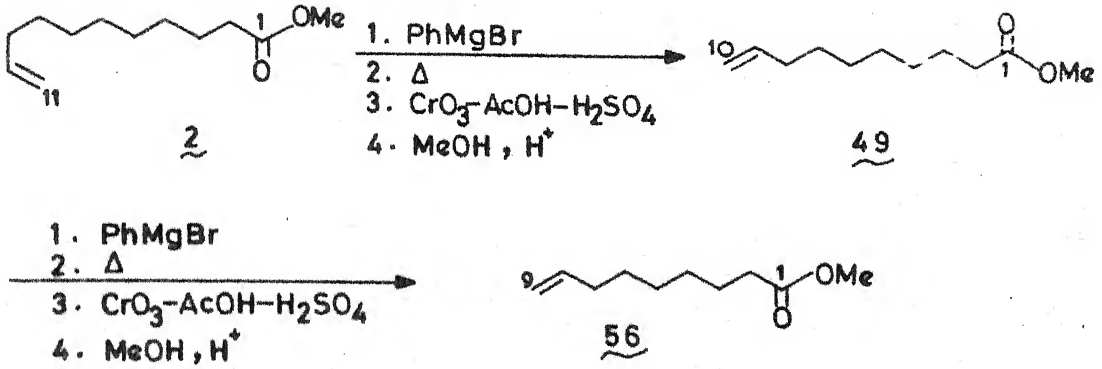
54 : bp 102°/0.05 torr;
ir: ν_{max}(neat)(cm^{-1}): 1740 (ester).
nmr: $\delta_{(CCl_4)}$: 2.25 (t, 4H, $-C\underline{H}_2-COOMe$), 3.6 (s, 6H, $-CH_2COOC\underline{H}_3$).

55 : bp 146°/ 0.1 torr;
ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1690 (carboxylic acid).
nmr: $\delta_{(CCl_4)}$: 2.25 (m, 4H, $-C\underline{H}_2-COOMe$, $-C\underline{H}_2-COOH$), 3.6 (s,3H, $-CH_2-COOC\underline{H}_3$), 11.6 (s, 1H, $-COO\underline{H}$).

56 : ir: ν_{max}(neat)(cm^{-1}): 1740 (ester). 1640 (double bond).
nmr: $\delta_{(CCl_4)}$: 2.1 (m, 4H, $CH_2=CH-C\underline{H}_2-$, $-C\underline{H}_2-COOMe$), 3.5 (s, 3H, $-COOC\underline{H}_3$), 4.85 (m, 2H, $C\underline{H}_2=CH-$), 5.65 (m, 1H, $CH_2=C\underline{H}-$).

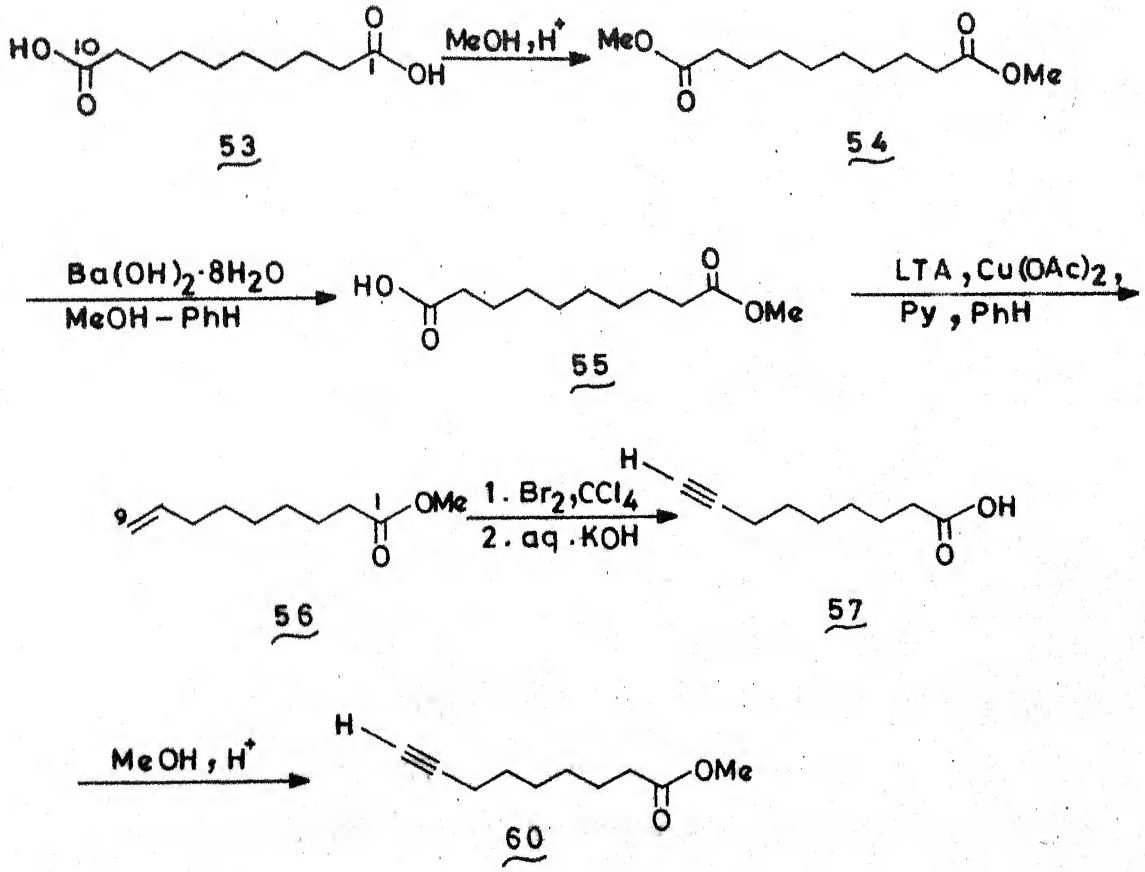
57 : bp 102-105°/0.1 torr;
ir: ν_{max}(neat)(cm^{-1}): 3300 ($-C\equiv C-H$), 2120 ($-C\equiv C-$), 1710 (carboxylic acid).

CHART C.IX



2 49 56

CHART C.X



53 54 55 56 57 60

nmr: $\delta_{(CCl_4)}$: 1.72 (t, 1H, H-C≡C-), 2.1 (m, 4H, H-C≡C-CH_2-, -CH_2-COOH), 9.88 (s, 1H, -CH_2-COOH).

Prior to the discovery of the facile decarboxylative elimination, endeavours were directed at the preparation of the olefinic ester 56 from sebacic acid monomethyl ester 55 by Hunsdiecker reaction to the bromide 58 and elimination (vide infra). The complexity of the above sequence warranted a preparation of an authentic sample of 56 and this was accomplished by sequential Barbier Wieland degradation of 2 (Chart C.IX).

Methyl decane 1,10-dioic acid monoester (55) was transformed to methyl 9-bromo nonanoate (58) (69%) by reaction with Br_2-HgO in CCl_4 under illumination with a tungsten lamp.[72] Surprisingly, dehydrobromination of 58 with potassium t-butoxide in dry t-butanol, under conditions recommended for exclusive terminal π formation,[73] gave complex mixtures with the olefinic component amounting to 29% and which largely consisted of the internal olefin 59 rather than the desired 56 (NMR) (Chart C.XI).

Another route to methyl non 8-ynoate (60) explored was by Wittig reaction on methyl 8-oxo octanoate-generated from 49 by isomerisation and π cleavage - with Ph_3P=CHCl followed by KO^tBu treatment. The yields were not satisfactory.

Chart C.XI

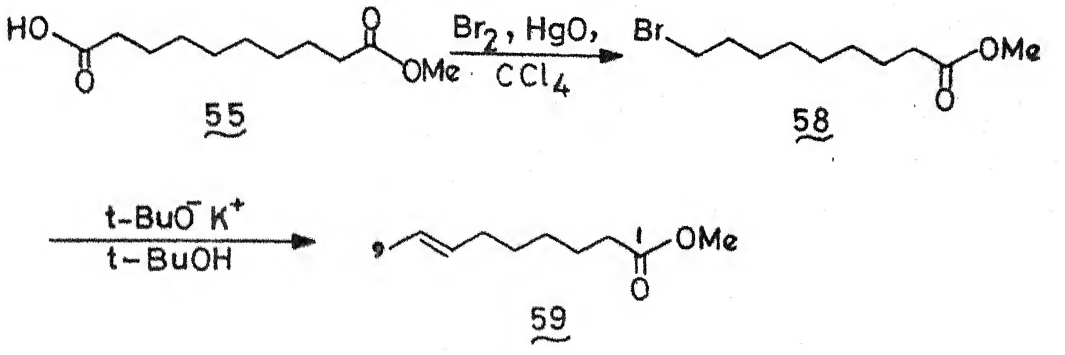
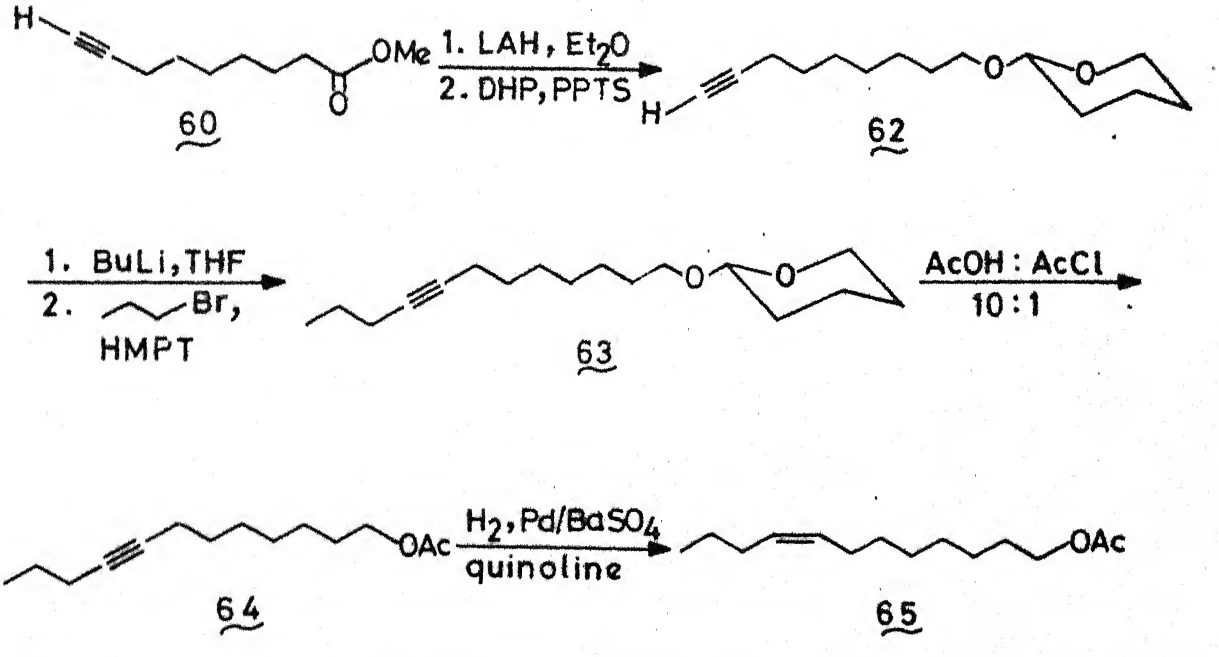


Chart C.XII



The preparation of 1-tetrahydropyranyloxy non 8-yne (62)

Methyl non 8-ynoate (60), prepared, in 86% yield, by esterification of 57, was reduced with LAH to the alcohol 61 (96%), and then protected with dihydropyran using PPTS as catalyst to give 1-tetrahydropyranyloxy non 8-yne (62) (91%) (Chart C.XII).

---

60 : bp 62°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 3300 (-C≡C-H), 2110 (-C≡C-), 1735(ester).

nmr: $\delta_{(CCl_4)}$: 1.75 (t, 1H, H-C≡C-), 2.2 (m, 4H, H-C≡C-CH_2-, -CH_2-COOMe), 3.6 (s, 3H, -COOCH_3).

61 : ir: ν_{max}(neat)(cm^{-1}): 3460 (hydroxyl), 3300 (-C≡C-H), 2110 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.72 (t, 1H, H-C≡C-), 2.05 (m, 2H, H-C≡C-CH_2-), 3.52 (t, 3H, -CH_2-OH).

62 : ir: ν_{max}(neat)(cm^{-1}): 3300 (-C≡C-H), 2110 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.7 (t, 1H, H-C≡C-), 2.08 (m , 2H, H-C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O-), 4.5 (s, 1H,).

1-Tetrahydropyranyloxy non 8-yne (62) could be anticipated to be a useful synthon for the preparation of insect sex pheromones of the type, R-CH=CH-$(CH_2)_6$-CH_2X. This has been illustrated with

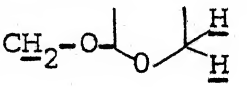
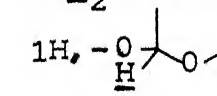
the synthesis of the sex pheromone related to the insect species, Grapholita molesta.

The synthesis of 1-acetoxy dodec (Z) 8-ene (65), the sex pheromone of Grapholita molesta*,74

1-Tetrahydropyranyloxy dodec 8-yne (63), prepared in 89% yield by alkylation of 62 with n-propyl bromide, was directly transformed with AcOH:AcCl::10:1, to 1-acetoxy dodec 8-yne (64) (83%) and then, stereoselectively hydrogenated to 1-acetoxy dodec (Z) 8-ene (65) (97%), the pheromone related to Grapholita molesta (Chart C.XII) (overall yield from 62, 71.7%).

---

63 : ir: ν_{max}(neat) (cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.98 (t, 3H, $\underline{CH_3}-CH_2-$), 2.0 (m, 4H, $-\underline{CH_2}-C\equiv C-\underline{CH_2}-$), 3.0-4.0 (m, 4H, $-\underline{CH_2}-O-$ ), 4.5 (s, 1H, ).

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* A chemical sex pheromone isolated in pure form from the abdominal tips of the female oriental fruit moth, Grapholita molesta, was identified as (Z) 8-dodecenyl acetate. In field tests the synthetic pheromone attracted more than 1200 males from apple trees. The best results were obtained with 10-200 µg of the compound absorbed on polyethylene. The male moths responded by fanning their wings, twirling, pausing with the abdominal tips curved upwards and opening and closing of the claspers, they appear to expose their scent pencils as if directing a male odour

64 : ir: ν_{max}(neat) (cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 1.95 (s, 3H, $-OCOC\underline{H}_3$), 2.1 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 4.0 (t, 2H, $-C\underline{H}_2-OCOCH_3$).

65 : ir: ν_{max}(neat) (cm^{-1}): 1735 (acetate).

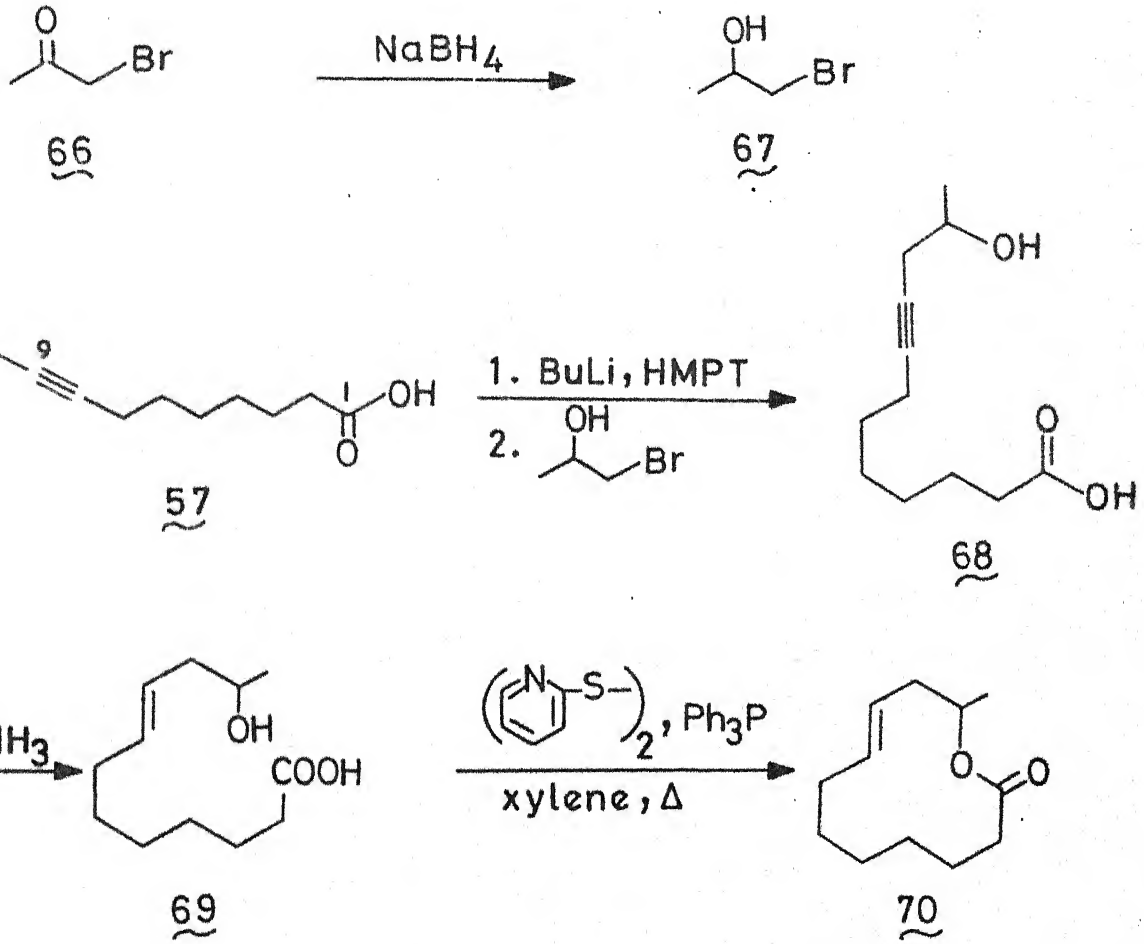
nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.92 (m, 7H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.9 (t, 2H, $-C\underline{H}_2OCOCH_3$), 5.28 (m, 2H, $-C\underline{H}=C\underline{H}-$).

Non 8-ynoic acid (57) and 1-tetrahydropyranyloxy non 8-yne (62) should be good synthons for the preparation of compounds that possess a 8,9 π bond. Of particular interest was the fact that methyl non 8-ynoate (60) derived from non-natural product precursors had been transformed to the macrolide, recifeiolide (70)[75]. Thus, since 60 has already been converted to recifeiolide, the present work relating to the transformation of castor oil to 60, constitutes also the synthesis of recifeiolide in a formal sense. Nevertheless, having a ready access to 60 from sebacic acid (53), it was considered possible to effect an independent synthesis of recifeiolide, using a more effective synthon that could directly lead to the needed $-CH_2CH(Me)OH$ system, since, in the earlier work, this moiety was generated from a methylene skipped π unit by selective functionalization.

The synthesis of 11-hydroxy dodec (E) 8-enoic acid lactone (70, recifeiolide)[76], a naturally occurring macrolide from Cephalosporium recifei

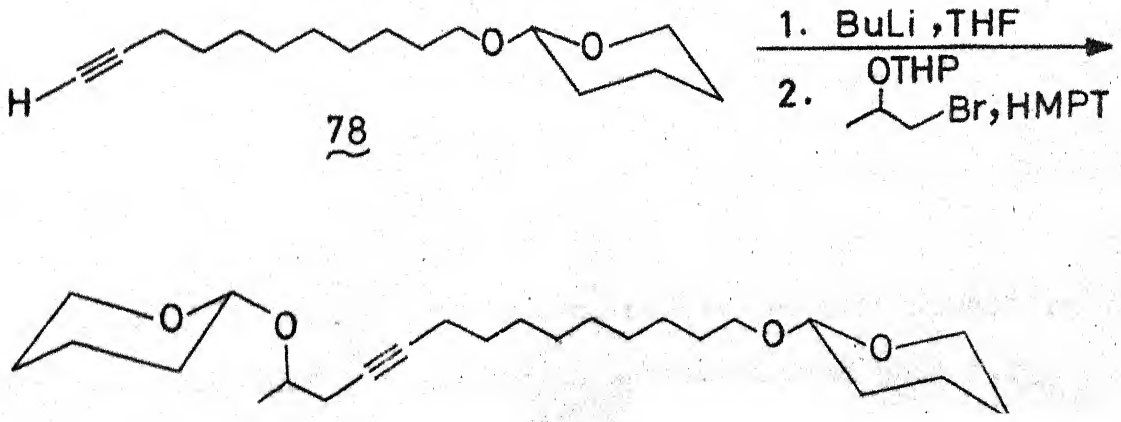
Selective alkylation of the dilithium salt of non 8-ynoic acid (57) with 1-bromo 2-hydroxy propane (67) - prepared by the sodium borohydride reduction of bromoacetone (66) in 58% yield (Chart C.XIII.) - in HMPT, gave 11-hydroxy dodec 8-ynoic acid (68). In spite of variation in the conditions of the reaction as well as the quantities of material involved, the desired alkylation proceeded poorly and resulted in a complex mixture which defied isolation of pure 68. From ir it was estimated that the alkylation had taken place to the extent of ~ 50%. Efforts at this alkylation with the fully O-protected synthon 71 gave even poorer yields in the alkylation step (vide infra). The mixture containing 68 was treated with sodium-liquid ammonia and the in situ generated E-olefin 69 cyclised via the dipyridyl disulfide ester method.[77] Careful column chromatography gave small amounts of recifeiolide (Chart C.XIII) whose spectral properties were identical to that of an authentic sample. This series of experiments establishes the feasibility of the synthesis of recifeiolide via the novel procedure involving acetylide alkylation. However, a more effective synthon is needed for the acetylide alkylation, as this step alone has made the present synthesis notional rather than practical.

Chart C.XIII



66 67 57 68 69 70

Chart C.XIV



78 72

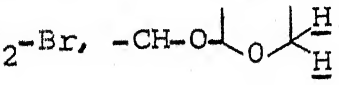
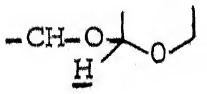
In the early experiments, the protected 2-tetrahydropyranyloxy 1-bromo propane, derived from 67, was used for the acetylide alkylation studies. Surprisingly, in the model system, 1-tetrahydropyranyloxy undec 10-yne (78), the alkylation with this synthon proceeded satisfactorily leading to the diprotected acetylenic alcohol 72. In sharp contrast, attempts to effect such an alkylation with undec 10-ynoic acid (75) gave very poor results (Chart C.XIV).

---

70 : ir: ν_{max}(neat) (cm^{-1}): 1740 (lactone).

nmr: $\delta_{(CCl_4)}$: 1.4 (d, 3H, CH_3-CH-O-C(=O)-), 2.58 (m, 6H, $-CH_2-CH=CH-CH_2-$, $-CH_2-CO-$), 5.24 (m, 1H, $CH_3-CH(-O-C(=O)-)$), 5.5 (m, 2H, -CH=CH-).

71 : ir: ν_{max}(neat) (cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.25 (t, 3H, $CH_3-CH(OTHP)CH_2Br$), 3.2-4.1 (m, 5H, $CH_3-CH-CH_2-Br$, -CH-O- ), 4.65 (s, 1H, -CH-O- ).

The surprisingly clean decarboxylative elimination of methyl decane 1,10-dioic acid monoester (55) to methyl non 8-enoate (56) made it logical to study the general nature of this transformation, and particularly, with reference to incorporating this for a terminal π to a lower terminal π change, for which no clean

procedure is presently available. It was also felt that it would be advantageous to select a substrate that would lead to a known product which had been identified as a useful synthon. The logical choice was, therefore, methyl undec 10-enoate (2).

The preparation of the key synthon methyl dec 9-enoate (49) from 2 by a terminal $\pi \longrightarrow$ lower terminal π change

Methyl undec 10-enoate (2) was subjected to treatment with diborane under carefully controlled conditions. Direct Jones' oxidation of the resulting trialkylborane gave, in 49% yield, methyl undecane 1,11-dioic acid monoester (73). Treatment of 73 with lead tetraacetate under conditions developed for the 55 $\longrightarrow$ 56 change, gave, cleanly, in 36% yield, methyl dec 9-enoate (49), identical to an authentic sample prepared by the classical Barbier Wieland degradation of 2 (Chart C.XV). The 2 $\longrightarrow$ 49 change not only attests to the general nature of this degradation but, also, constitutes the best method for the preparation of 49. Parenthetically, 49 is a key prostaglandin synthon and its transformation product, namely, 1-tetrahydropyranyloxy dec 9-yne has been established as a useful synthon for the practical preparation of several insect sex pheromones of the type, $R\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}CHXY$.[69]

73: ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1710 (carboxylic acid).

CHART C. XV

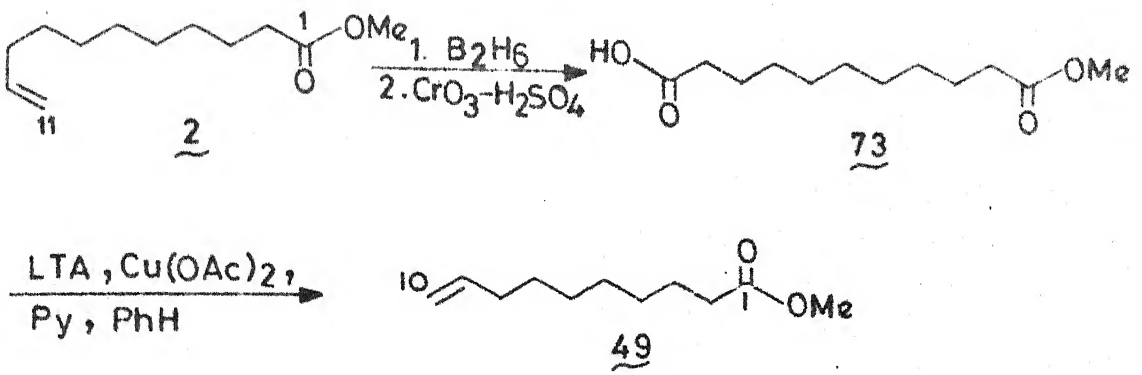
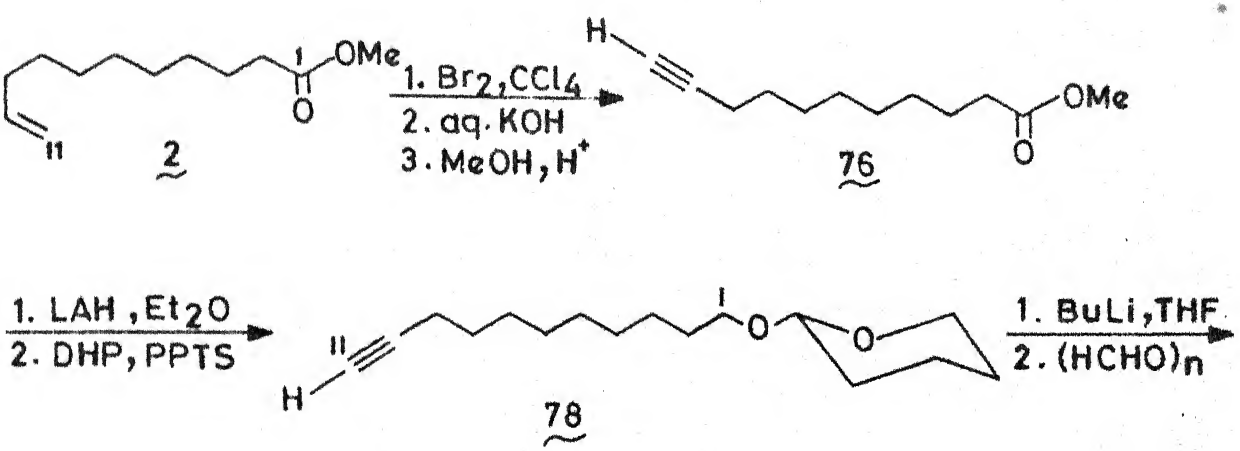
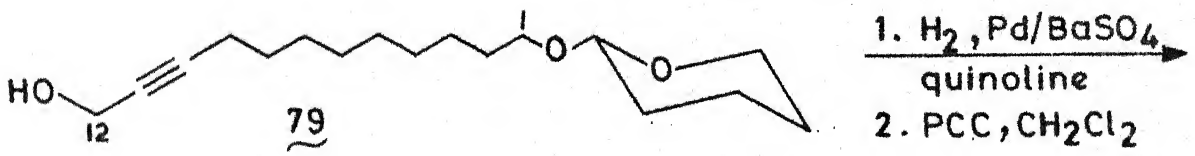
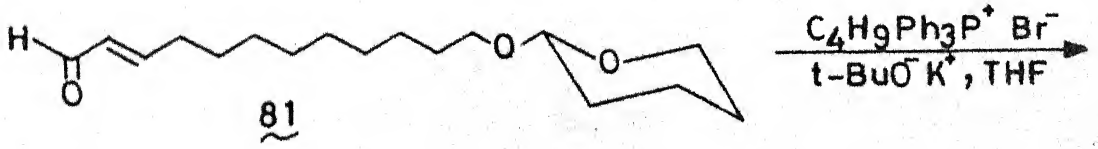
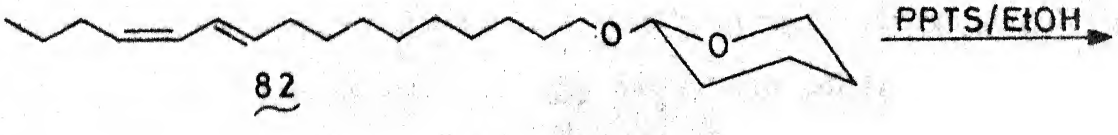


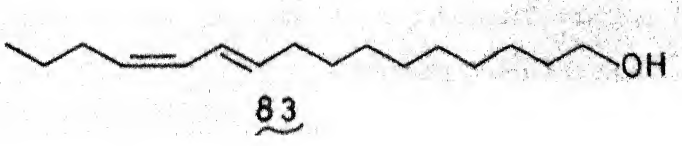
CHART C. XVI











49: bp 60-61°/0.3 torr;

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.68 (s, 3H, $-COOC\underline{H}_3$), 4.9 (m, 2H, $C\underline{H}_2=CH-$), 5.8 (m, 1H, $CH_2=C\underline{H}-$).

Several methods to prepare 11-hydroxy dodec (E) 8-enoic acid, the immediate precursor to recifeiolide (70), from synthons derived from castor oil were attempted without success. These include the possible synthesis of, from 2, methyl undeca 8,10-dienoate and methyl 11-hydroxy dodec 9-enoate, from 49, methyl 11-hydroxy dodec 8-enoate, methyl 12-trichloromethyl 11-hydroxy dodec 8-enoate and methyl 11-oxo dodec 8-enoate.

Thus far, in the present work, the strategy employed for the synthesis of insect sex pheromones involved the direct union of the acetylide head segment with an appropriate hydrophobic tail moiety. It was felt that this strategy could be modified for the synthesis of insect sex pheromones possessing conjugate π systems or methylene skipped π systems by effecting the union of the two segments through a carbon element, that could, at will, be easily transformed to the required oxidation state. It was envisaged that CH_2O could be the coupling unit which would lead to a β,γ-acetylenic alcohol via acetylide addition. Such a rationale led to, in the present work, the synthesis of

1-tetrahydropyranyloxy 12-hydroxy dodec 10-yne (79) and the illustration of its synthetic potential by transformation to the insect sex pheromone, bombykol.

The synthesis of 1-tetrahydropyranyloxy 12-hydroxy dodec 10-yne (79)

Methyl undec 10-enoate (2) was transformed to the dibromide 74 (100%) which, on carefully controlled treatment with aqueous KOH, gave undec 10-ynoic acid (75) (50%). Compound 75 was converted to 1-tetrahydropyranyloxy undec 10-yne (78) by sequence, esterification, LAH reduction and DHP protection with an overall yield of 87%. Treatment of 78 with n-BuLi followed by paraformaldehyde gave 1-tetrahydropyranyloxy 12-hydroxy dodec 10-yne (79) in 64% yield (Chart C.XVI).

---

75 : bp 112-115°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1710 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, H-C≡C-), 2.2 (m, 4H, H-C≡C-CH_2-, -CH_2-COOH), 11.2 (s, 1H, -COOH).

76 : bp 70°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1740(ester).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, H-C≡C-), 2.15 (m, 4H, H-C≡C-CH_2-, -CH_2COOMe), 3.54 (s, 3H, -COOCH_3).

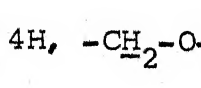
77 : bp 74-75°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 3310 (-C≡C-H), 2120 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.8 (t, 1H, H-C≡C-), 2.1 (m, 2H, H-C≡C-CH_2-), 3.55 (t, 3H, -CH_2-OH).

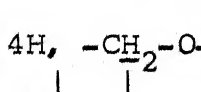
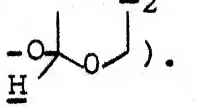
78 : bp 95°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.7 (t, 1H, H-C≡C-), 2.1 (m, 2H, H-C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O ), 4.45 (s, 1H, -O).

79 : bp 157-163°/0.05 torr;

ir: ν_{max}(neat)(cm^{-1}): 3420 (hydroxyl), 2280, 2220 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 2.39 (m, 2H, -C≡C-CH_2-), 2.9 (s, 1H, -CH_2-OH), 3.3-4.2 (m, 4H, -CH_2-O ), 4.26 (t, 2H, -CH_2-OH), 4.7 (s, 1H, -O ).

Compound 79 could be anticipated to be a versatile synthon. At its present oxidation state it could be effective for the synthesis of insect sex pheromones and other natural products having a methylene skipped π array. Alternately, 79 could be converted to the aldehyde which could then be a good precursor for systems having conjugated π-units. This aspect has been

illustrated with an efficient and highly stereoselective synthesis of bombykol.

The synthesis of 1-hydroxy hexadeca (E) 10, (Z) 12-diene (83, bombykol), the sex pheromone of Bombyx mori*,[78]

1-Tetrahydropyranyloxy 12-hydroxy dodec 10-yne (79) was stereoselectively hydrogenated over 5% Pd-$BaSO_4$ to the allylic alcohol 80 (96%) which was then oxidised with PCC to 1-tetrahydropyranyloxy 12-oxo dodec (E) 10-ene (81) (84%). Carefully controlled Wittig reaction of 81 with n-butyltriphenylphosphonium bromide gave 1-tetrahydropyranyloxy hexadeca (E) 10, (Z) 12-diene (82) (65%) which was de-protected with PPTS-EtOH to bombykol 83 (98%) (overall yield from 79, 33%) (Chart C.XVI).

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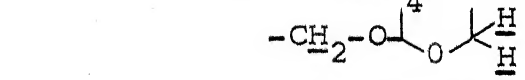
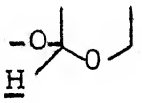
* The isolation of lepidopterous sex pheromones was pioneered by Butenandt and co-workers, who, after almost twenty years of experimental work, starting with the glands from 500,000 females, identified (10E, 12Z)-10,12 hexadecadien 1-ol (bombykol) as a pheromone of the female silkworm moth, Bombyx mori. The four geometric isomers of the conjugated dienol were synthesised for comparison with the physiochemical and biological properties of the natural pheromone and the 10E, 12Z isomer was found to be by far the most attractive to male silkworm moths in laboratory bioassays, leaving no doubt that the natural pheromone is mainly the 10E, 12Z isomer.

---

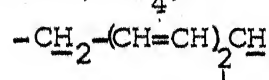
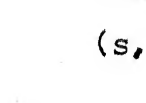
80 : bp 143-145°/0.07 torr;

ir: ν_{max}(neat)(cm^{-1}): 3425 (hydroxyl), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.9 (m, 2H, $-CH=CH-C\underline{H}_2-$), 2.9-4.0 (m, 7H,  , $-C\underline{H}_2-O\underline{H}$), 4.4 (s, 1H, ), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

81 : ir: ν_{max}(neat)(cm^{-1}): 1730 (aldehyde), 1640 (double bond), 1135, 1120, 1080, 1030 (-OTHP).

82 : ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.88 (t, 3H, $C\underline{H}_3-CH_2-$), 2.0 (m, 4H, $-C\underline{H}_2-(CH=CH)_2C\underline{H}_2-$), 3.0-4.0 (m, 4H, ), 4.4 (s, 1H, ), 4.95-6.3 (m, 4H, $-C\underline{H}=C\underline{H}-C\underline{H}=C\underline{H}-$).

83 : ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

500 MHz nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.5 -2.25 (m, 4H, $-C\underline{H}_2-(CH=CH)_2C\underline{H}_2-$), 2.88 (s, 1H, $-CH_2-O\underline{H}$), 3.62 (t, 2H, $-C\underline{H}_2-OH$), 5.35(dt,1H, $-CH_2-C\underline{H}=CH-CH=CH-$), 5.62 (dt,1H, $-CH_2-CH=CH-CH=C\underline{H}-$), 5.95(dd,1H, $-CH_2-CH=C\underline{H}-CH=CH-$), 6.3 (dd,1H, $-CH_2-CH=CH-C\underline{H}=CH-$).

GC analysis of 83 by Dr. David R. Hall, on 1.8m x 2mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene on Gas Chrom Q column showed that the diene contained 89.3% of the desired E,Z

isomer admixed with 1.6% Z,Z, 9.2% E,E and with only a very small amount of the Z,E isomer.

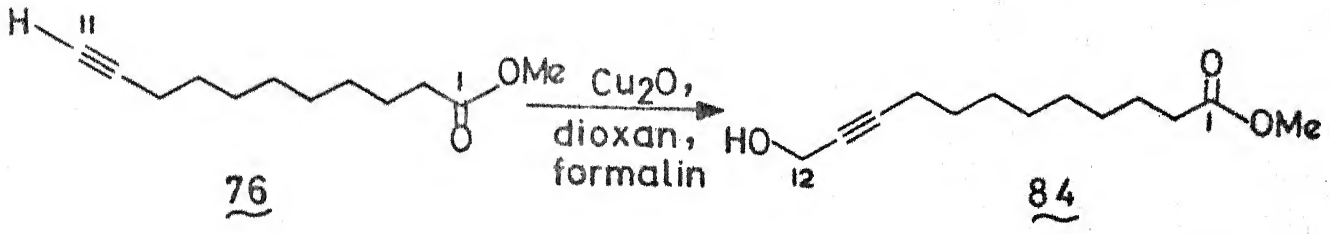
The present route to bombykol, by far, is the most attractive, in terms of the stereochemical purity and the availability of the starting materials.

In the early experiments, the hydroxymethylation was studied with methyl undec 10-ynoate (76). It was found that whilst the n-BuLi procedure is not compatible with the ester function, the desired hydroxymethylation could be achieved, in modest yields, using the classical procedure involving a copper acetylide species,[79] leading to methyl 12-hydroxy dodec 10-ynoate (84). Although 84 is not a preferred intermediate for the synthesis of bombykol, it should be of use for the preparation of compounds that possess an ester function. This is illustrated with a practical synthesis of the natural product, traumatin.

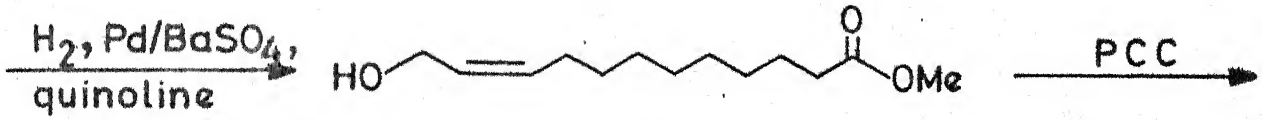
The synthesis of methyl 12-oxo dodec (E) 10-enoate (85, traumatin)[80]

Hydroxymethylation of methyl undec 10-ynoate (76) with cuprous oxide and formalin, in dioxan, gave methyl 12-hydroxy dodec 10-ynoate (84) (26%) which was selectively hydrogenated to the allylic alcohol 85 (90%). PCC oxidation of 85 gave methyl 12-oxo dodec (E) 10-enoate (86 , traumatin) (68%) (Chart C.XVII).

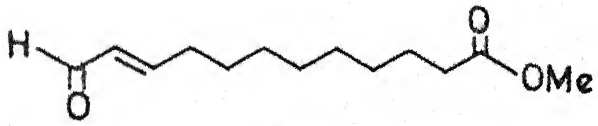
Chart C.XVII



76 84



85



86

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84 : bp 133-137°/0.4 torr;

ir: ν_{max}(neat)(cm^{-1}): 3460 (hydroxyl), 2280, 2220 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.21 (m, 4H, $-C\underline{H}_2-C\equiv C-$, $-C\underline{H}_2-COOCH_3$), 3.22 (s, 1H, $-CH_2-O\underline{H}$), 3.59 (s, 3H, $-COOC\underline{H}_3$), 4.08 (t, 2H, $-C\underline{H}_2-OH$).

85 : bp 92-96°/0.03 torr;

ir: ν_{max}(neat)(cm^{-1}): 3400 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.2 (m, 4H, $-C\underline{H}_2-COOCH_3$, $-CH=CH-C\underline{H}_2-$), 3.25 (s, 1H, $-CH_2-O\underline{H}$), 3.6 (s, 3H, $-COOC\underline{H}_3$), 4.03 (t, 2H, $-C\underline{H}_2-OH$), 5.45 (m, 2H, $-C\underline{H}=C\underline{H}-$).

86 : ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1720 (aldehyde).

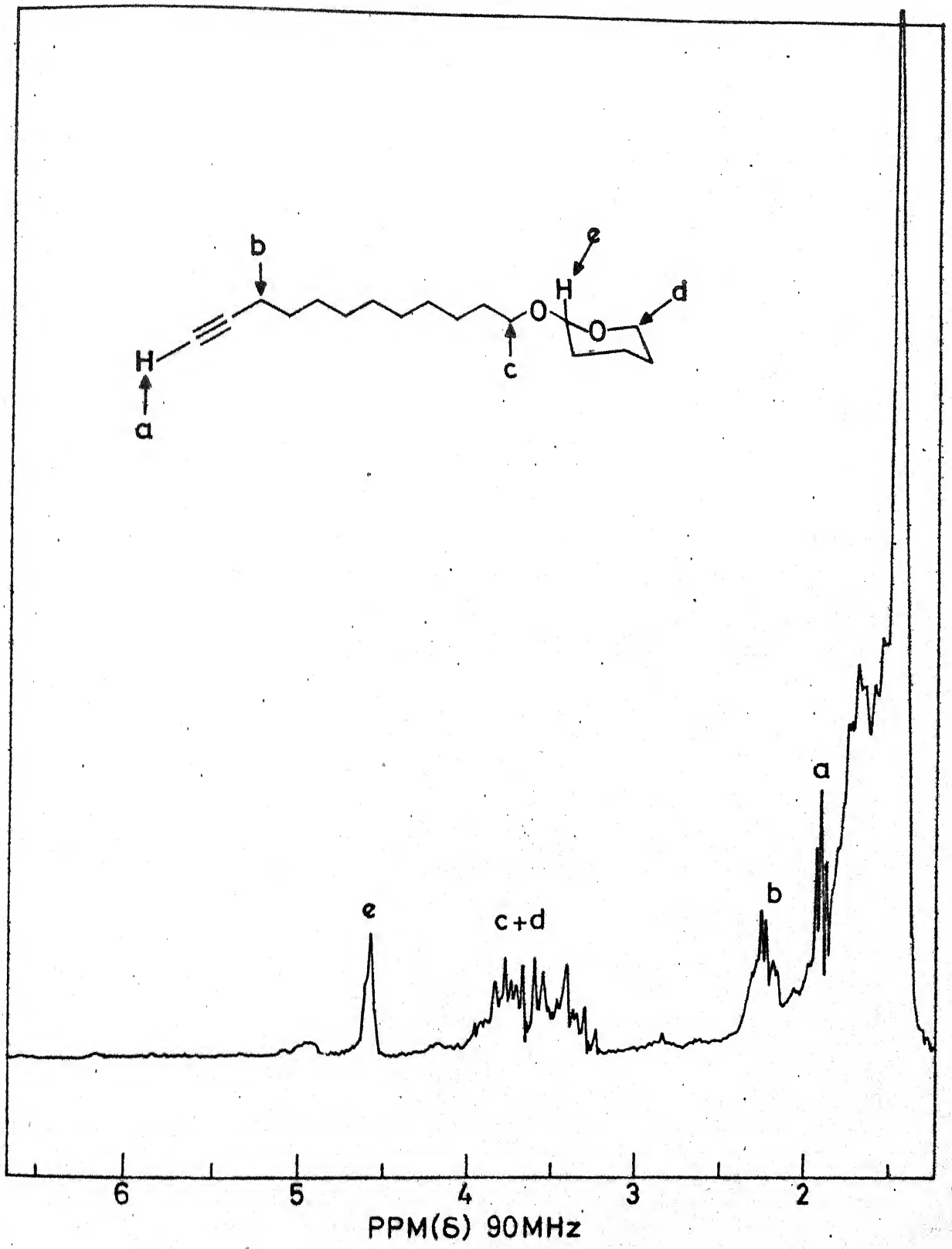
Semicarbazone : mp 130-132°.

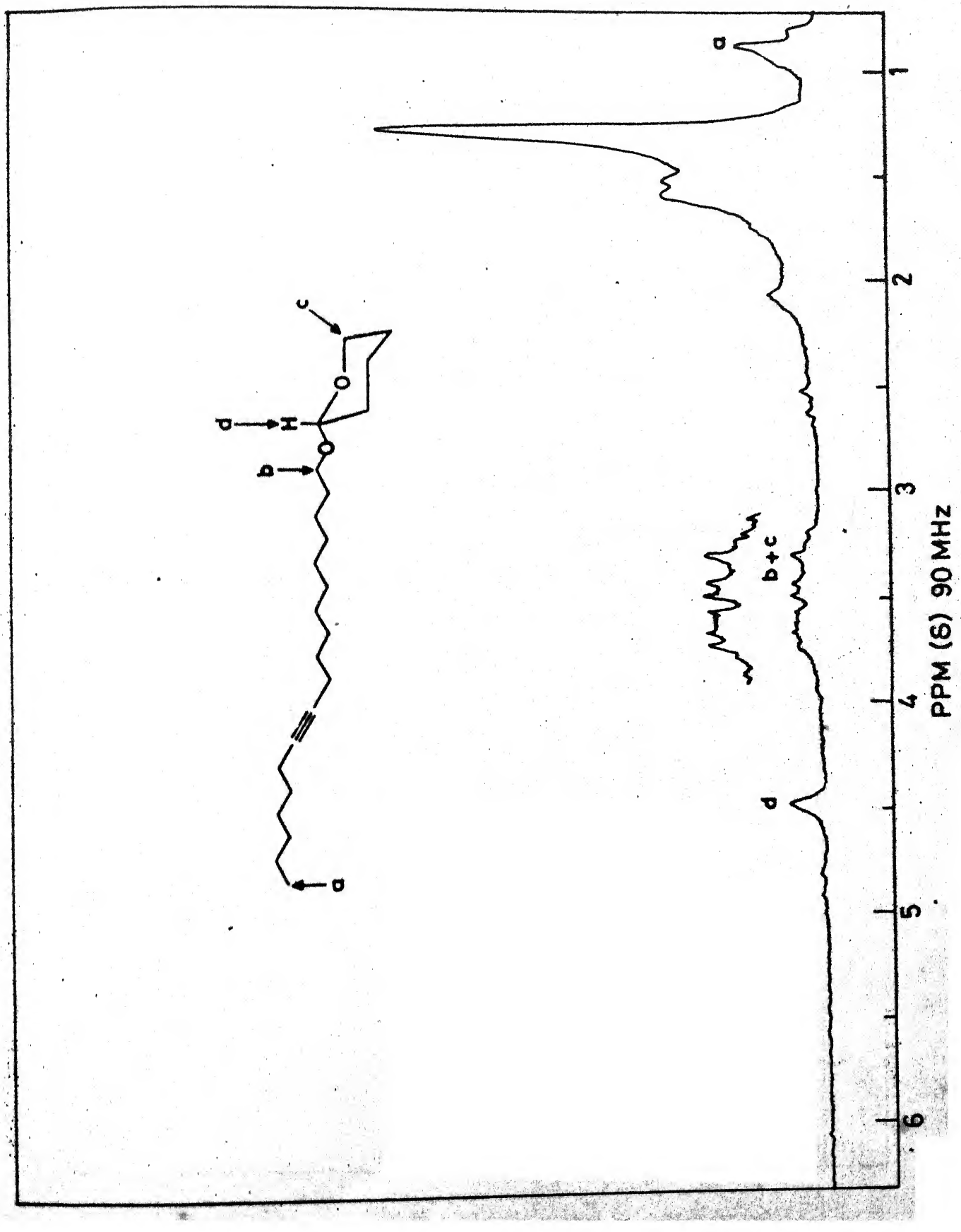
ir: ν_{max}(KBr): 3470 (-NH), 1740 (ester), 1690 (amide), 1660 (double bond).

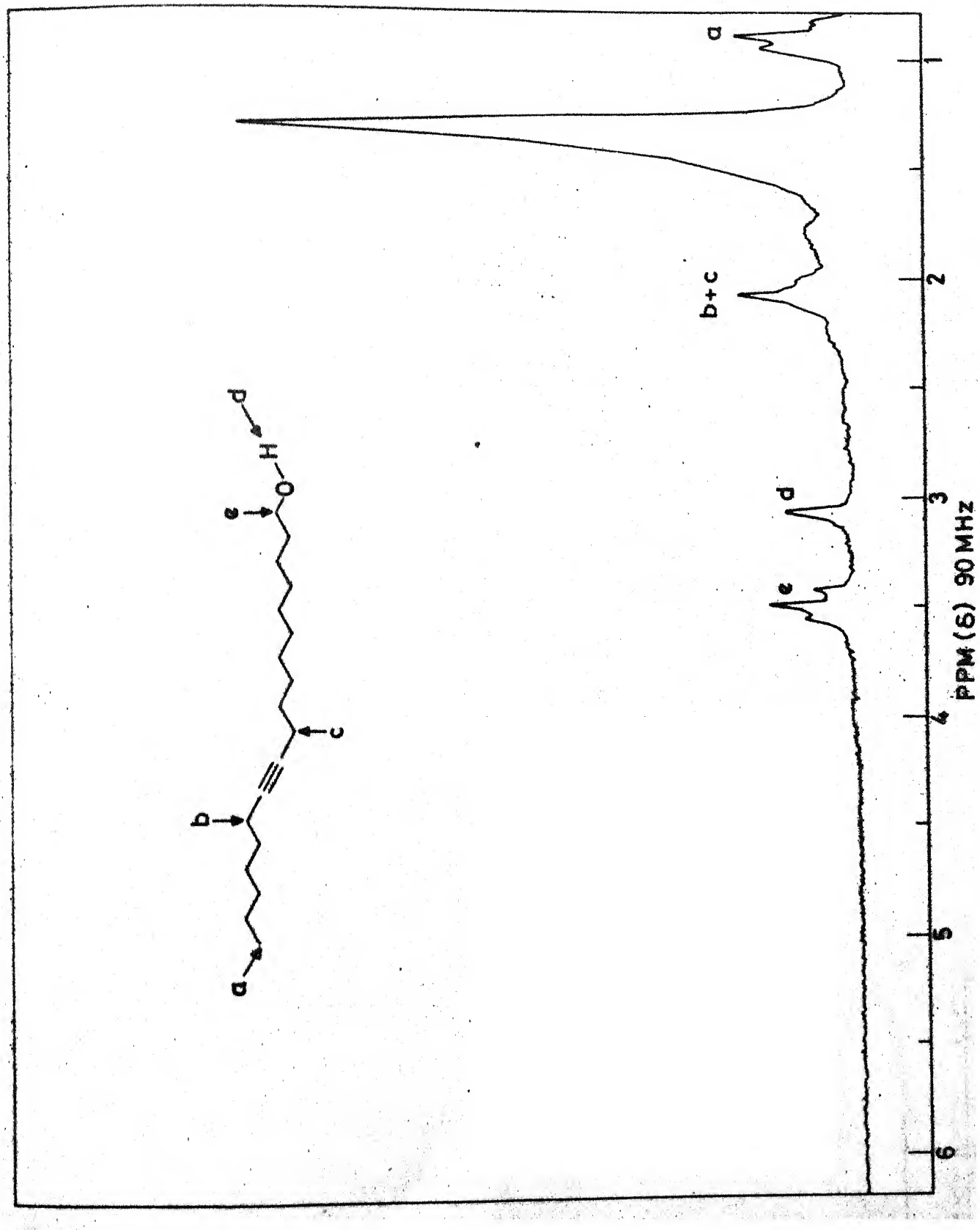
nmr: $\delta_{(CCl_4)}$: 9.65 (br, 1H, $-C\underline{H}=N-$), 7.40 (br, 1H, $-N\underline{H}$), 6.10 (br, 2H, $-CON\underline{H}_2$), 5.62 (br, 2H, $-C\underline{H}=C\underline{H}-$), 3.68 (s, 3H, $-COOC\underline{H}_3$), 2.25 (m, 4H, $-C\underline{H}_2-CH=CH-$, $-C\underline{H}_2-COOMe$).

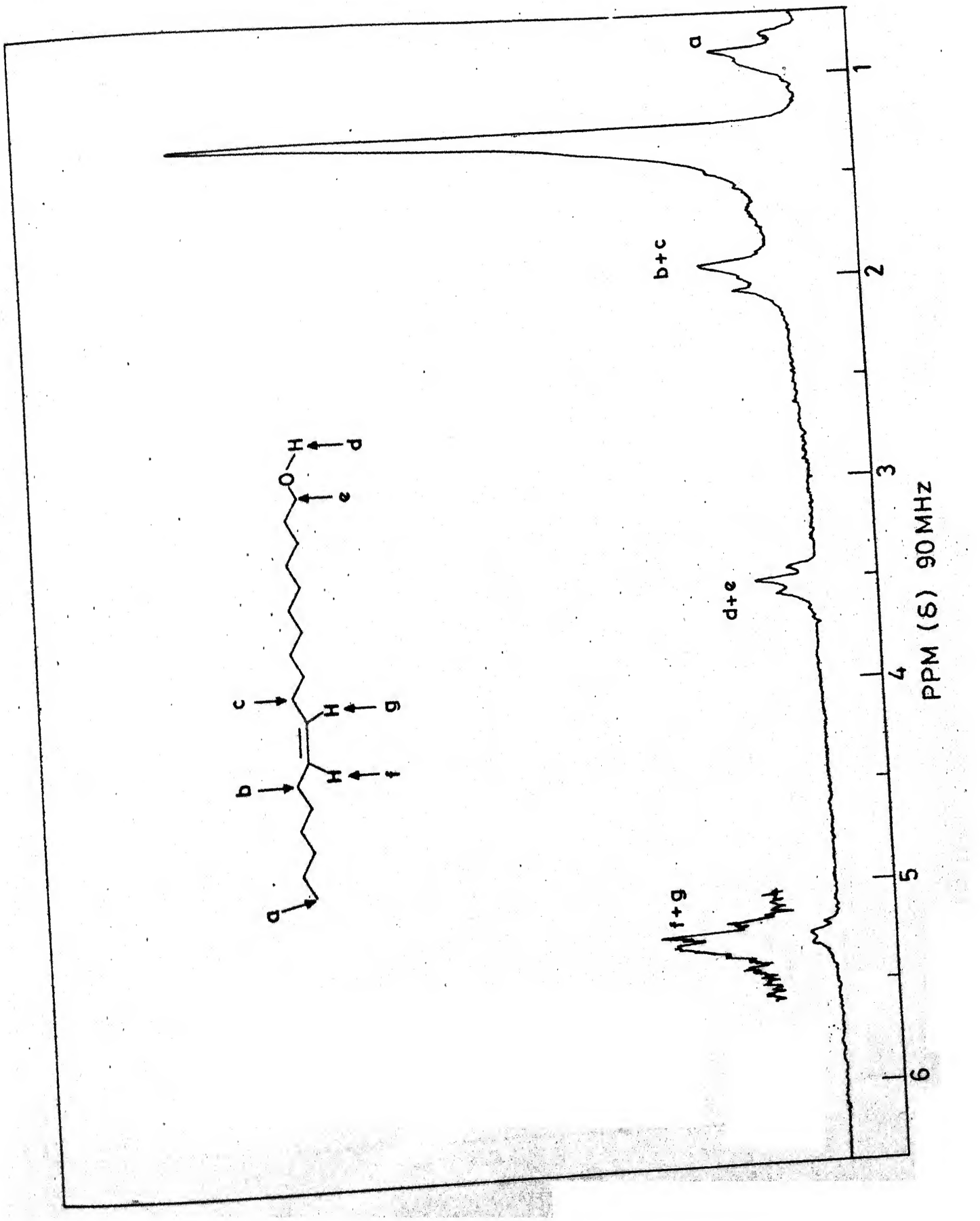
Parenthetically, the two immediate lower homologs of methyl 12-oxo dodec (E) 10-enoate (86), namely, methyl 11-oxo undec (E) 9-enoate and methyl 10-oxo dec (E) 8-enoate have been

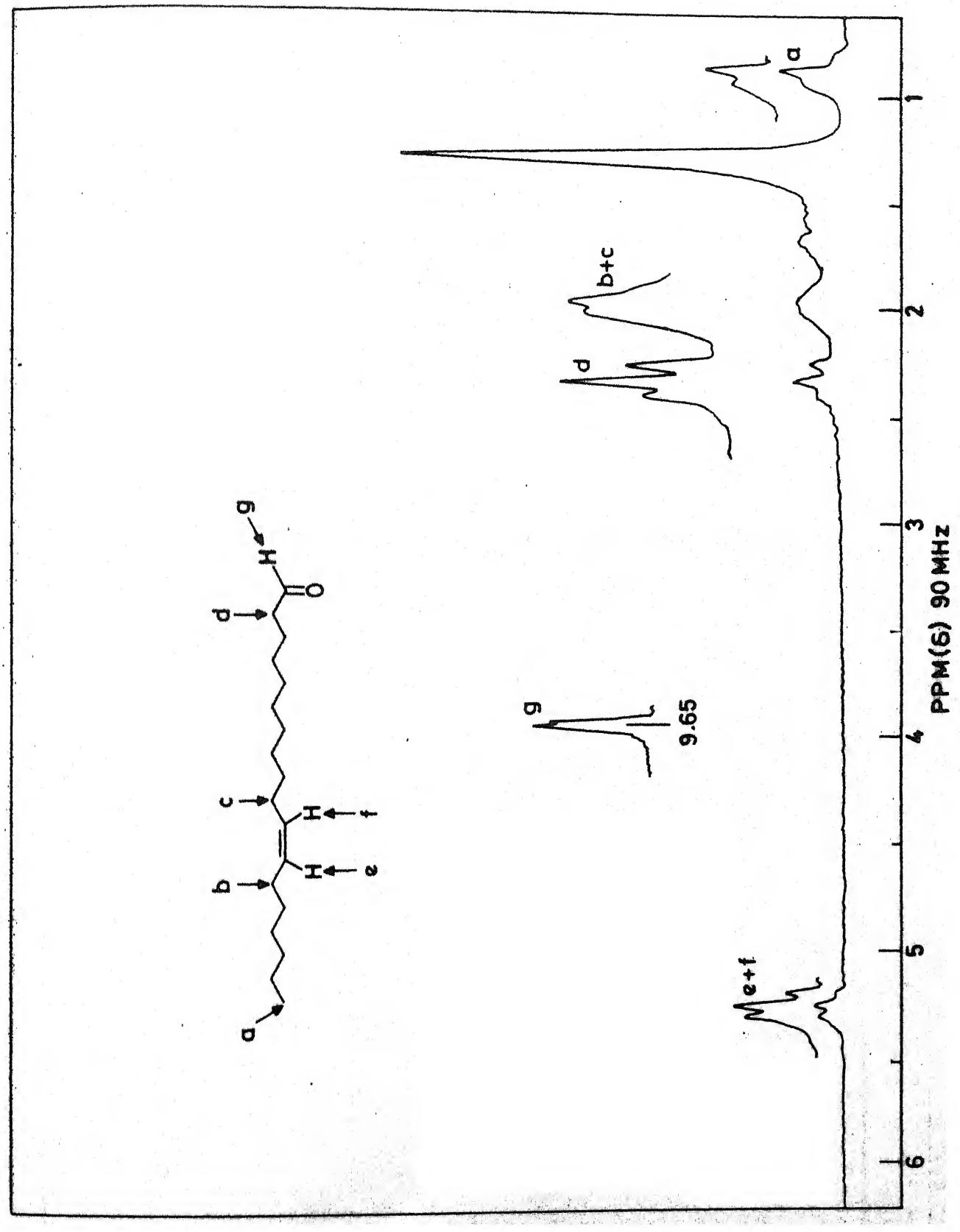
prepared by our group from castor oil, and they, in turn, have been transformed to prostaglandins and insect sex pheromones.[61,69]

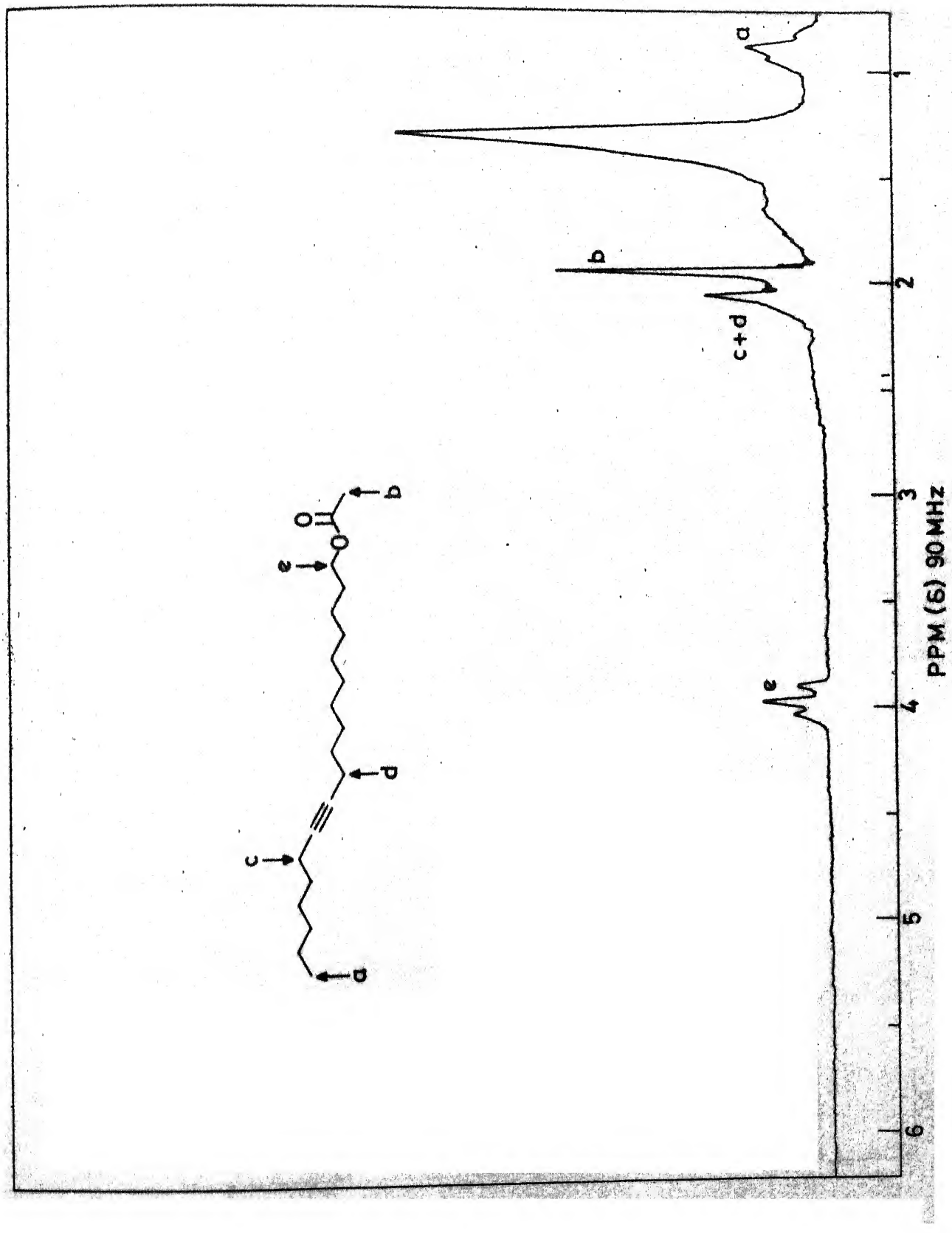

b
e
H
d
O
O
H
c
H
a
a
b
e
c+d
6
5
4
3
2
PPM(δ) 90MHz

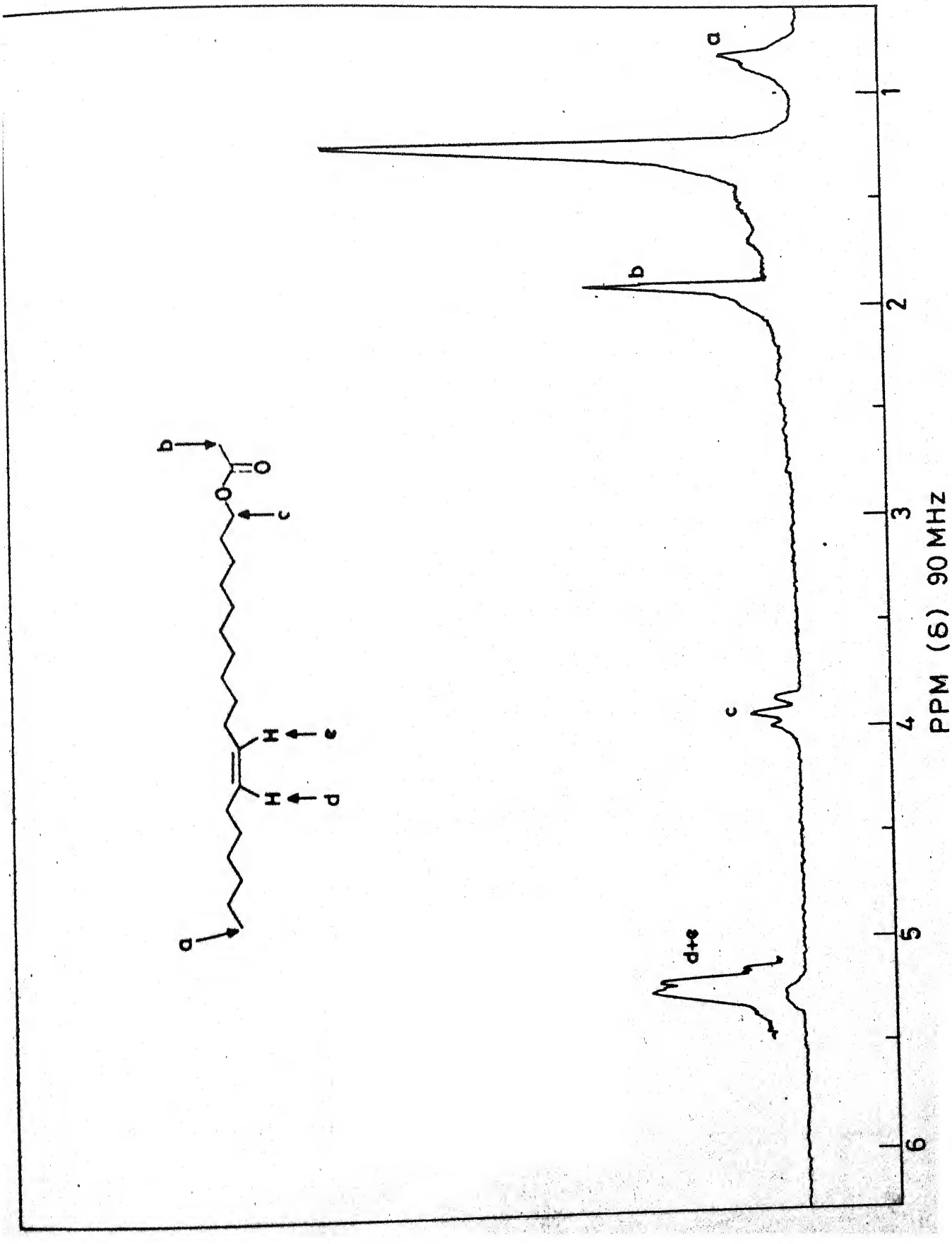

a
b+c
d
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
H
O
O

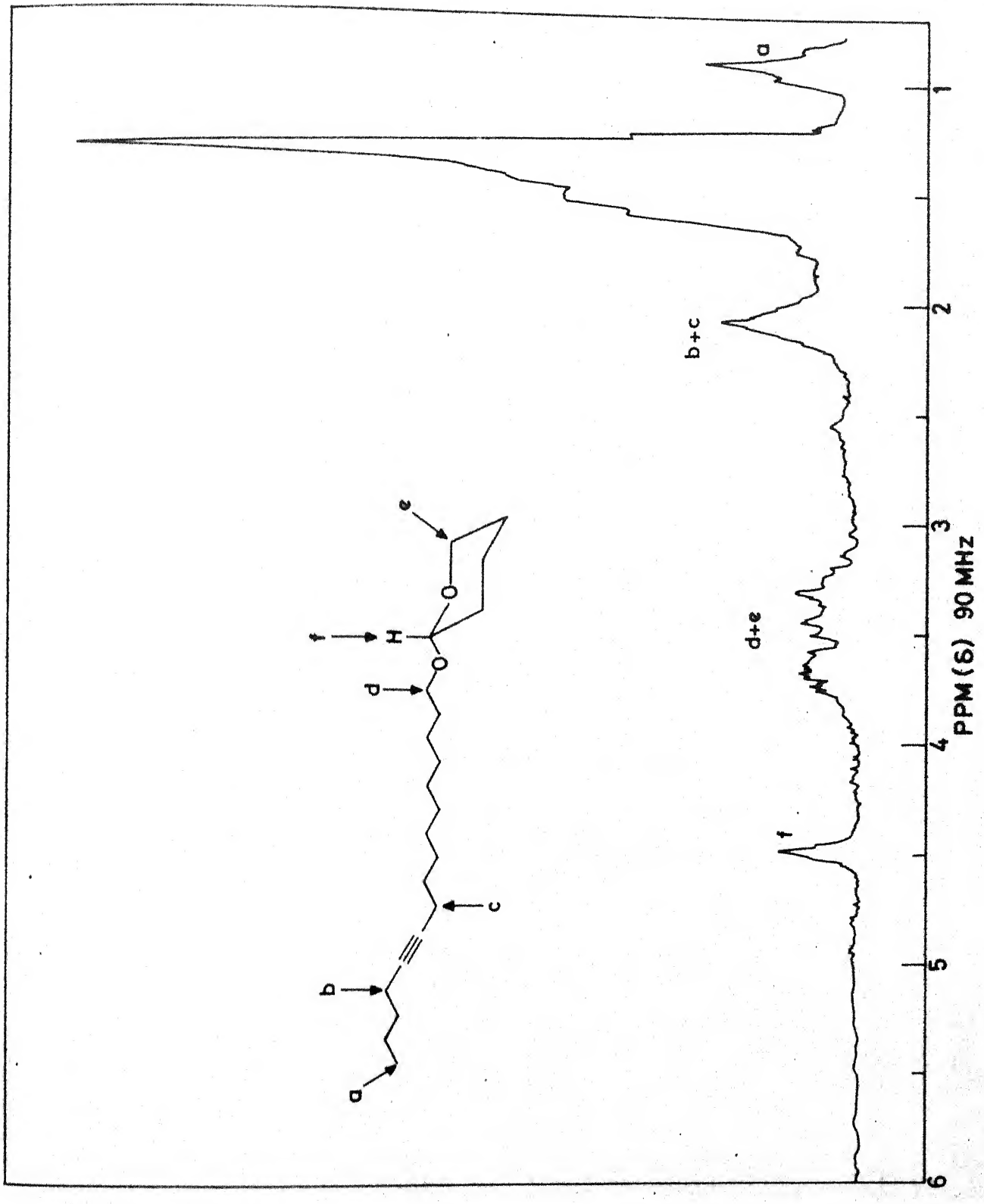

a
b+c
d
e
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
H
O

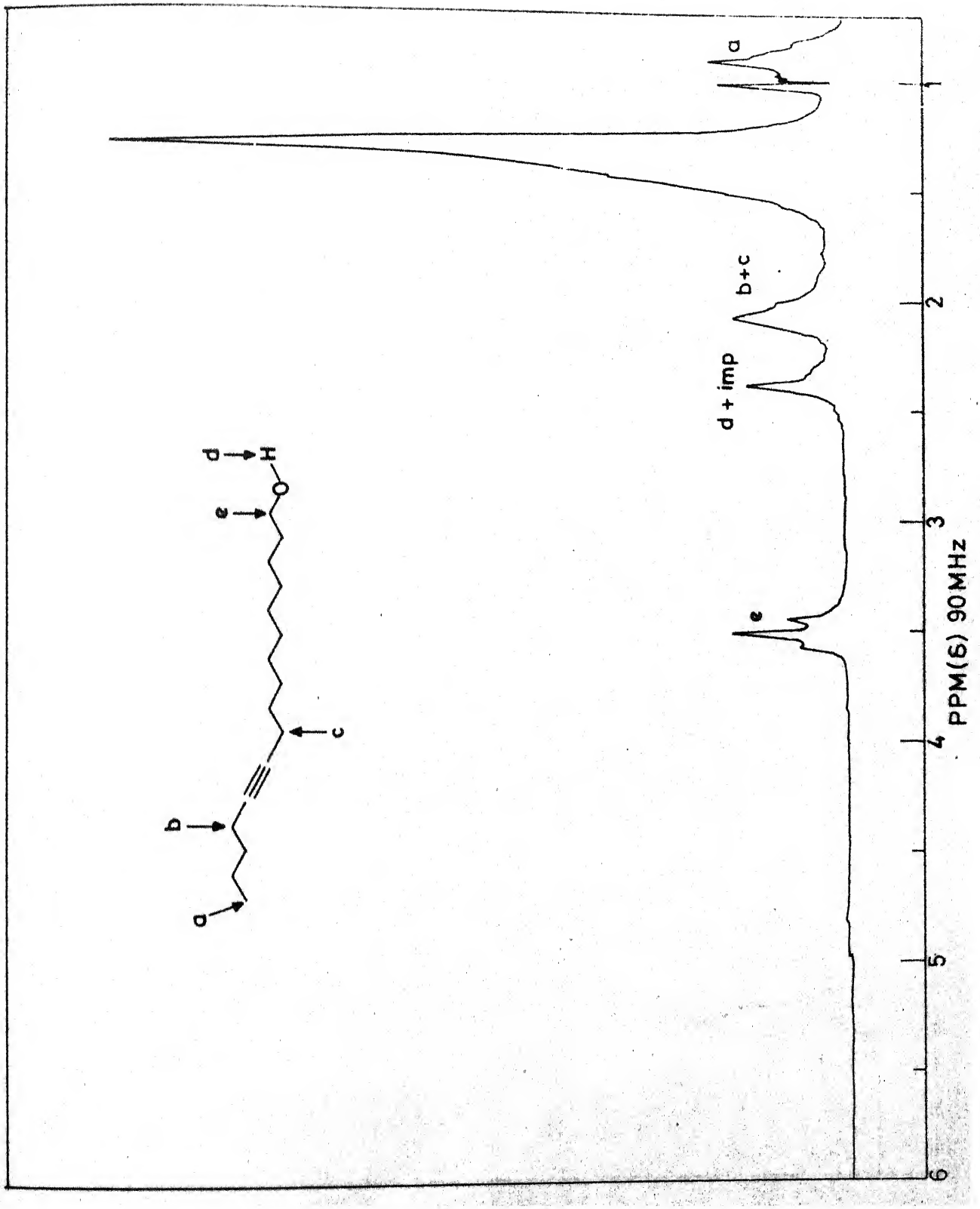

a
b+c
d+e
f+g
1
2
3
4
5
6
PPM (δ) 90MHz
a
b
c
d
e
f
g
H
O
H
H

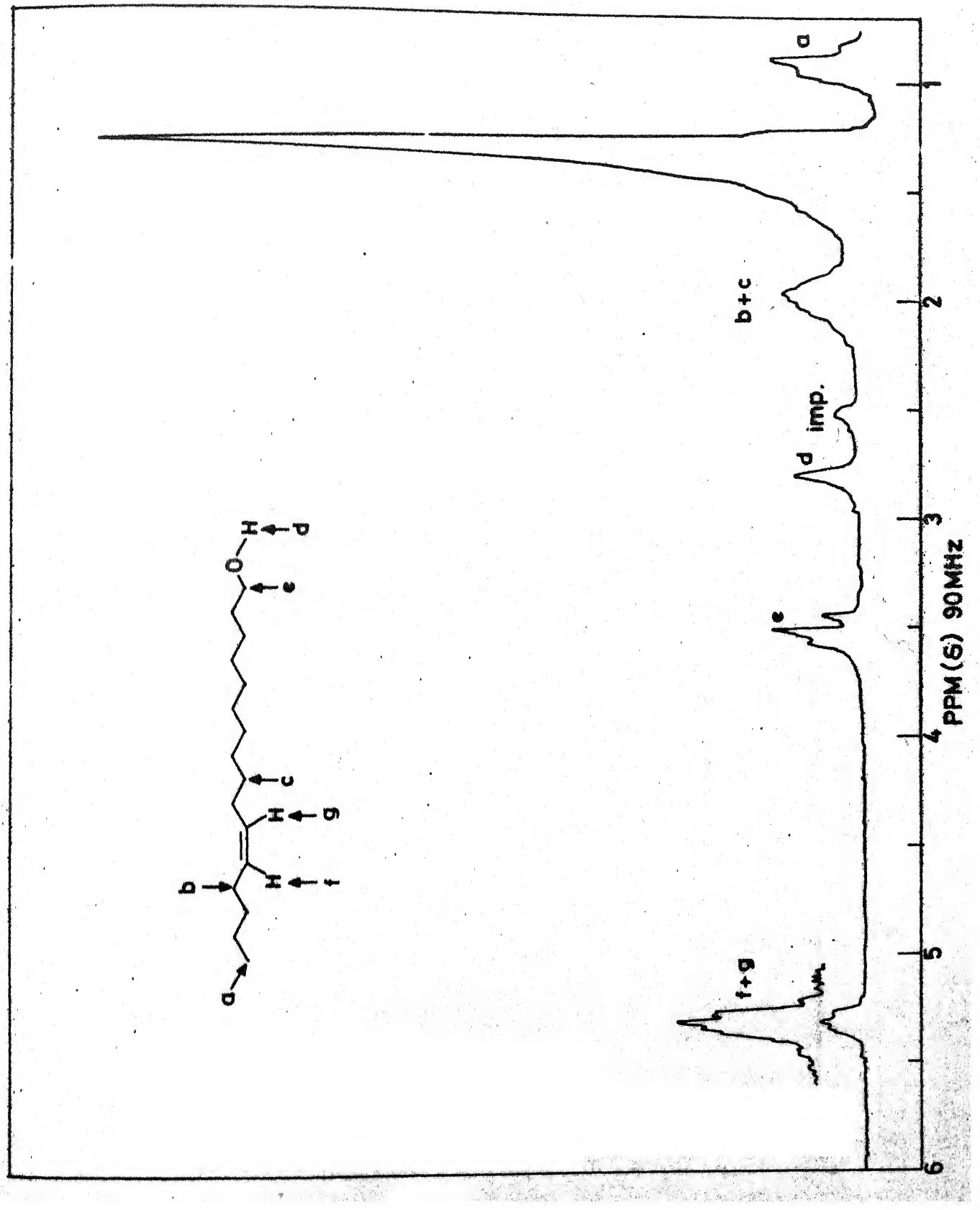

a
b+c
d
g
9.65
e+f
1
2
3
4
5
6
PPM(δ) 90 MHz
g
d
c
b
a
H
O
H
f
H
e

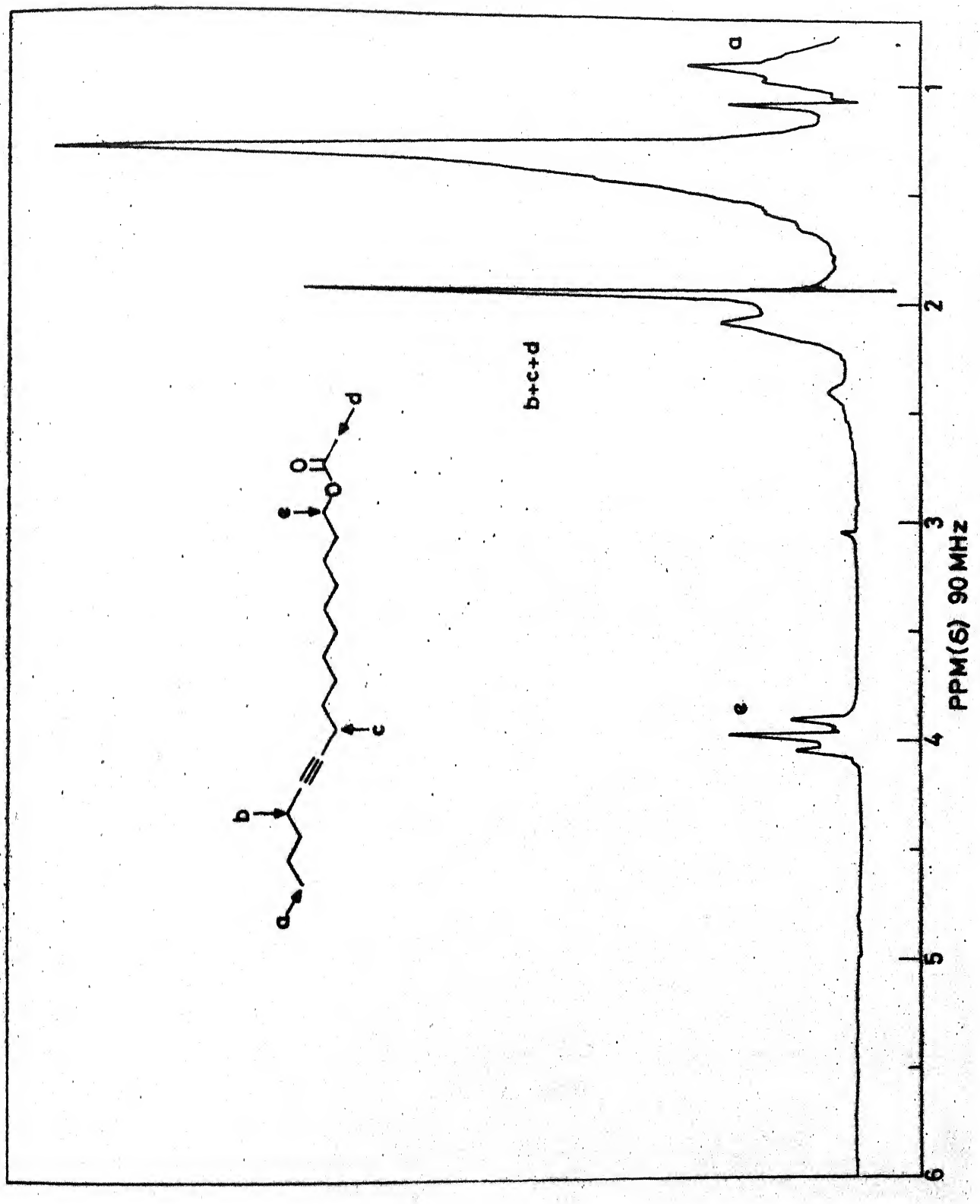

a
b
c+d
e
PPM (δ) 90 MHz
1
2
3
4
5
6
a
b
c
d
e

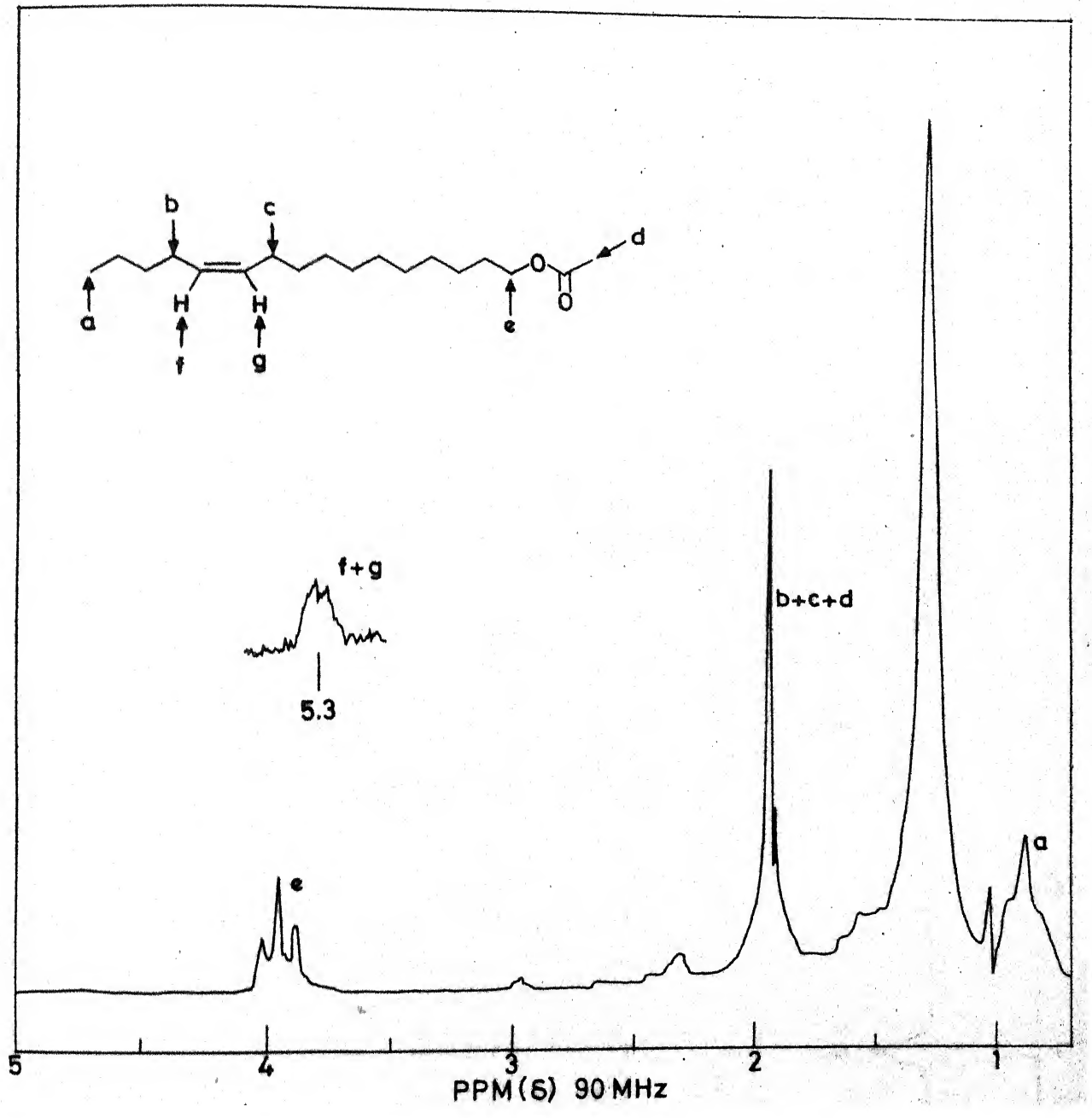

a
b
c
d+e
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
H
d
H
e

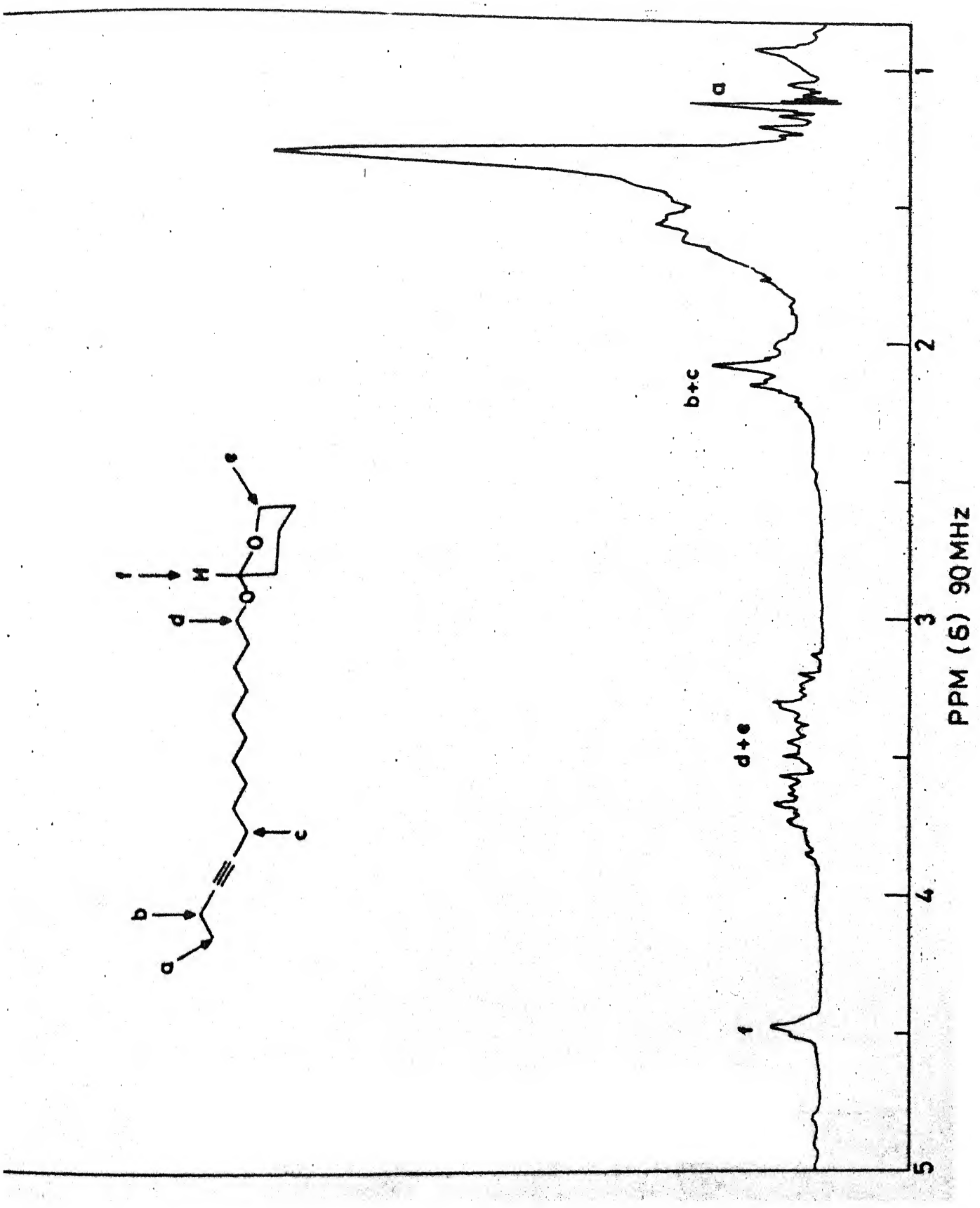

a
b+c
d+e
f
PPM (δ) 90 MHz
1
2
3
4
5
6
a
b
c
d
e
f
H
O
O

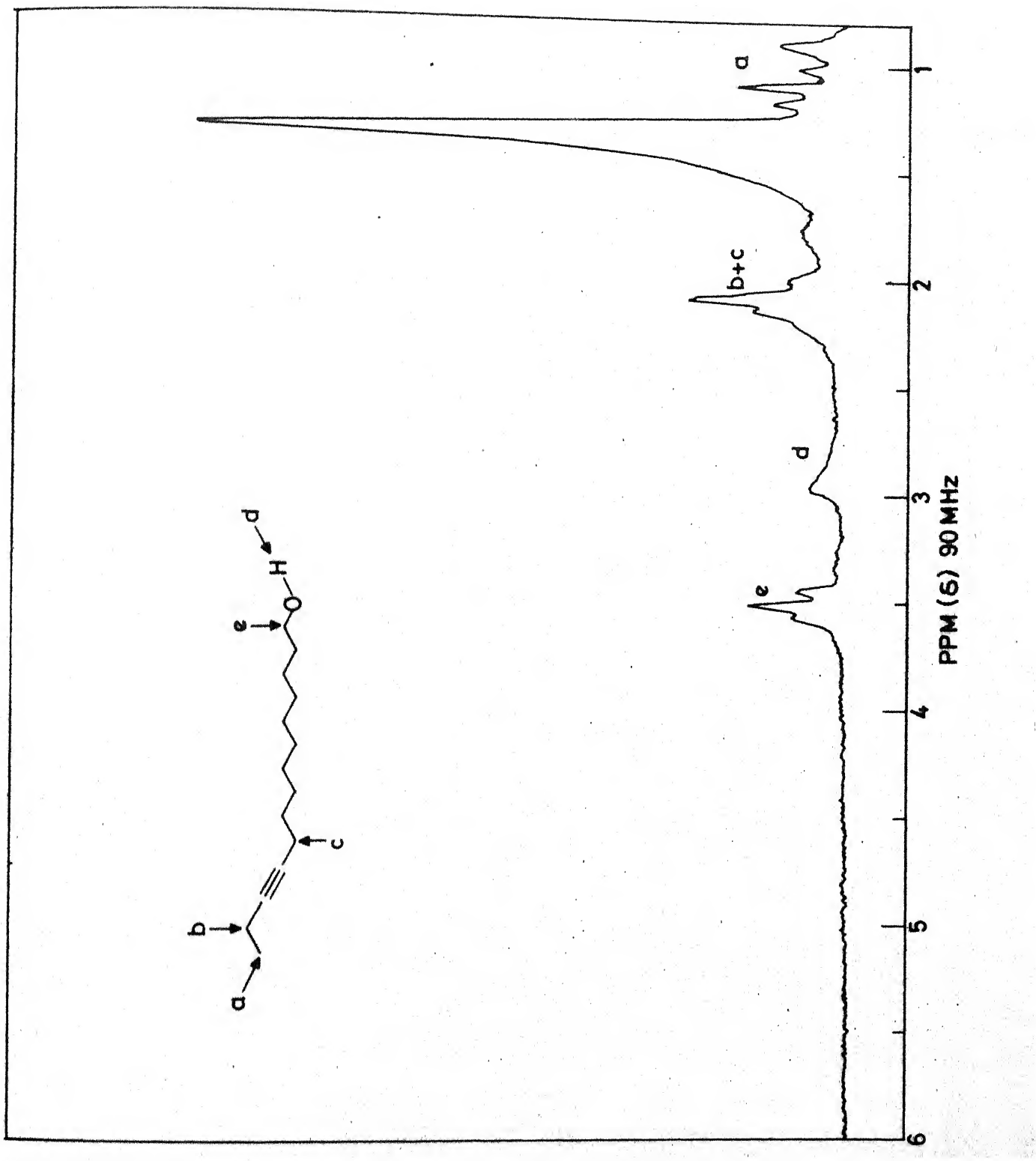

a
b+c
d + imp
e
1
2
3
4
5
6
PPM(δ) 90MHz
d
e
H
O
c
b
a

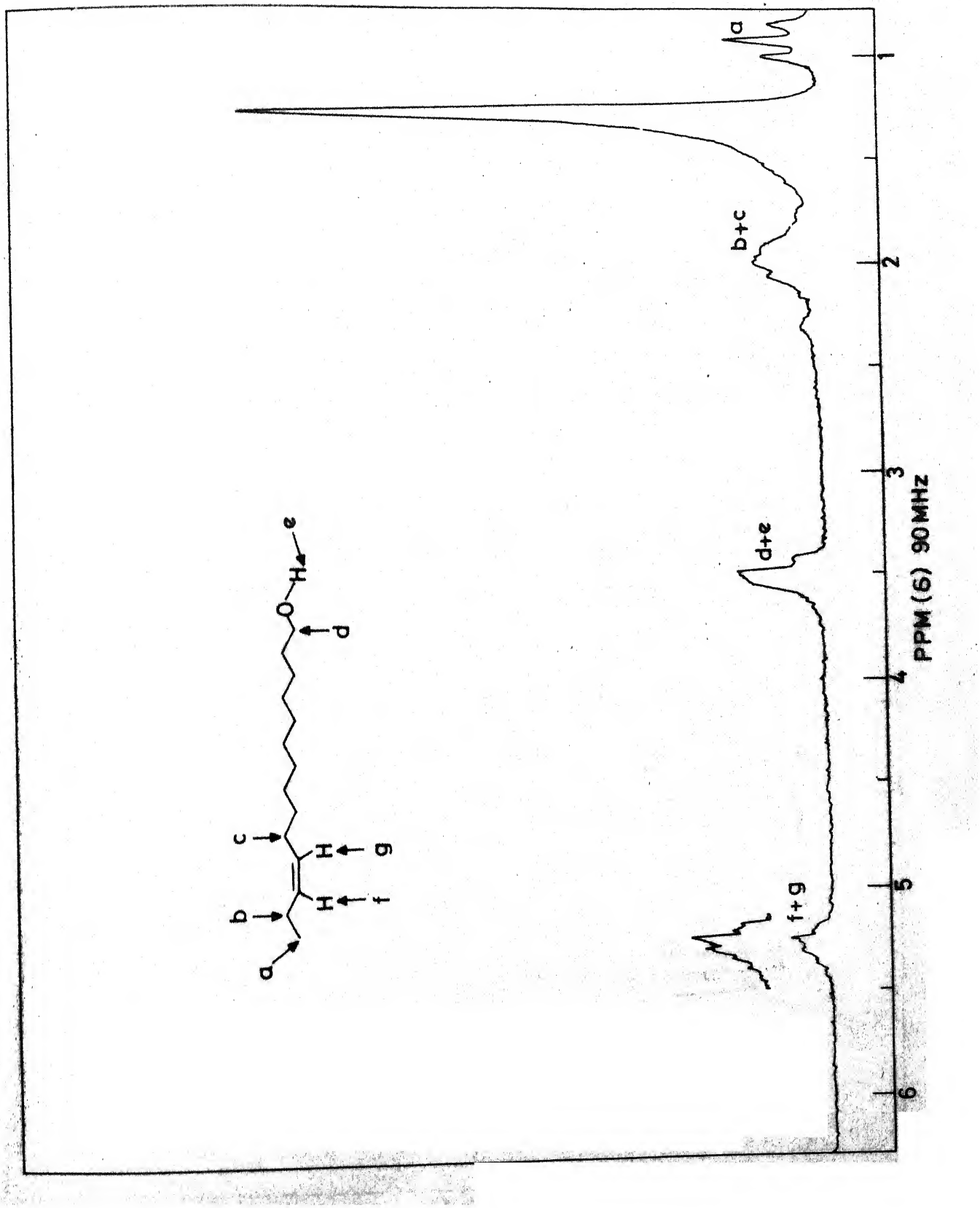

a
b+c
d imp.
e
f+g
1
2
3
4
5
6
PPM(δ) 90MHz
H
O
H
a
b
c
H
g
H
f
H
e
d

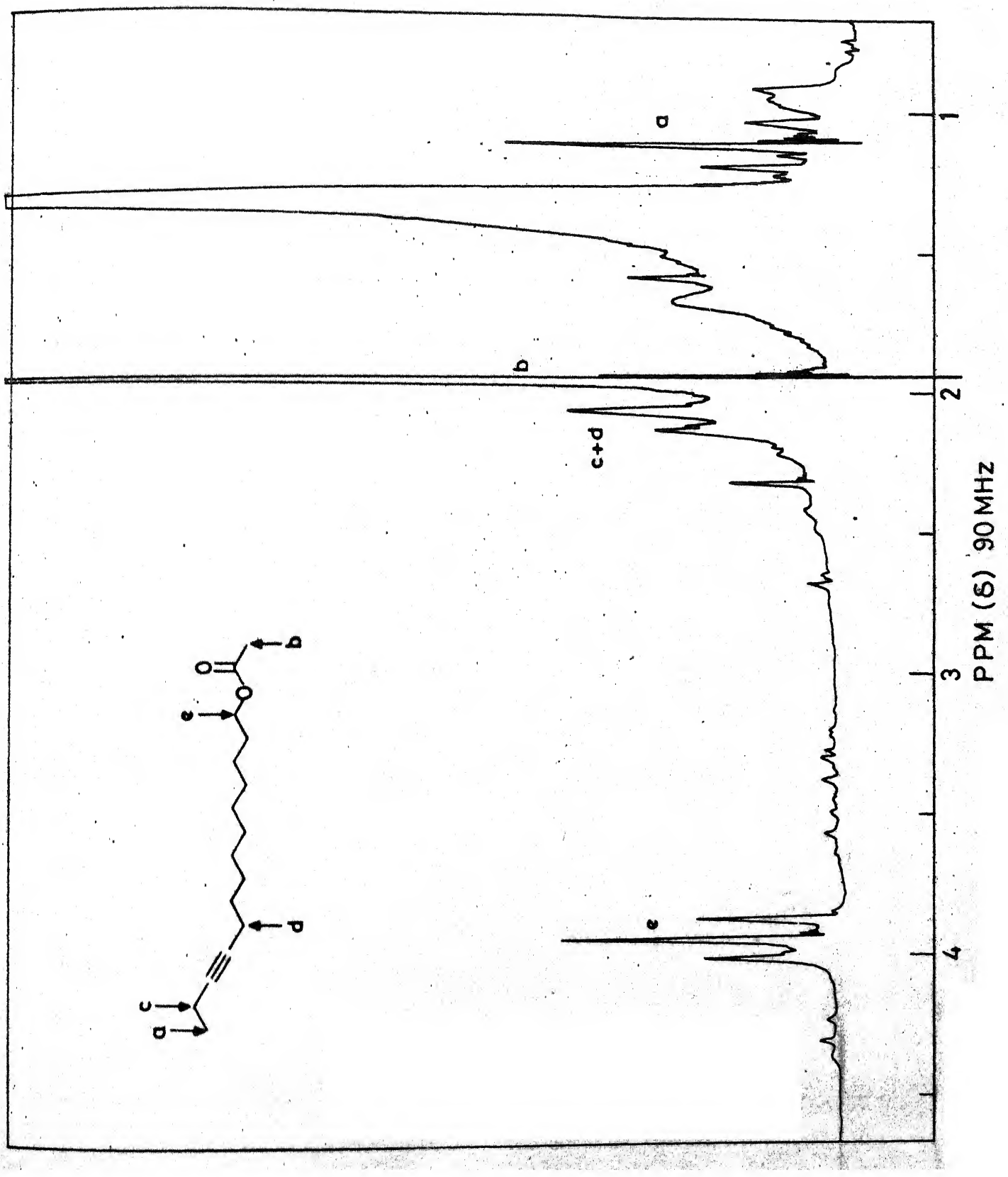

a
b+c+d
e
PPM(δ) 90 MHz
1
2
3
4
5
6
a
b
c
d
e
O
O

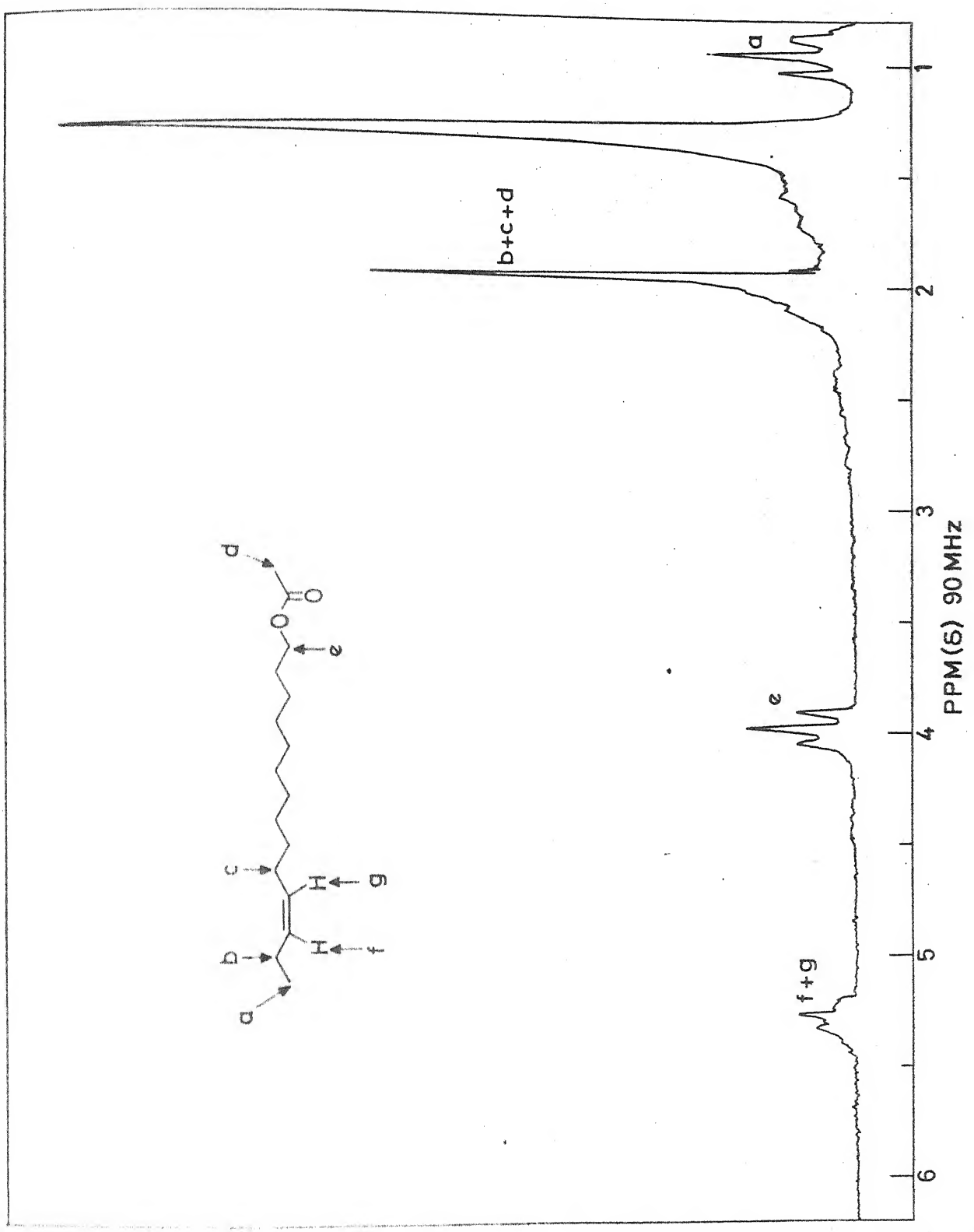

b
c
d
a
H
H
O
O
f
g
e
f+g
5.3
b+c+d
a
e
5
4
3
2
1
PPM(δ) 90 MHz

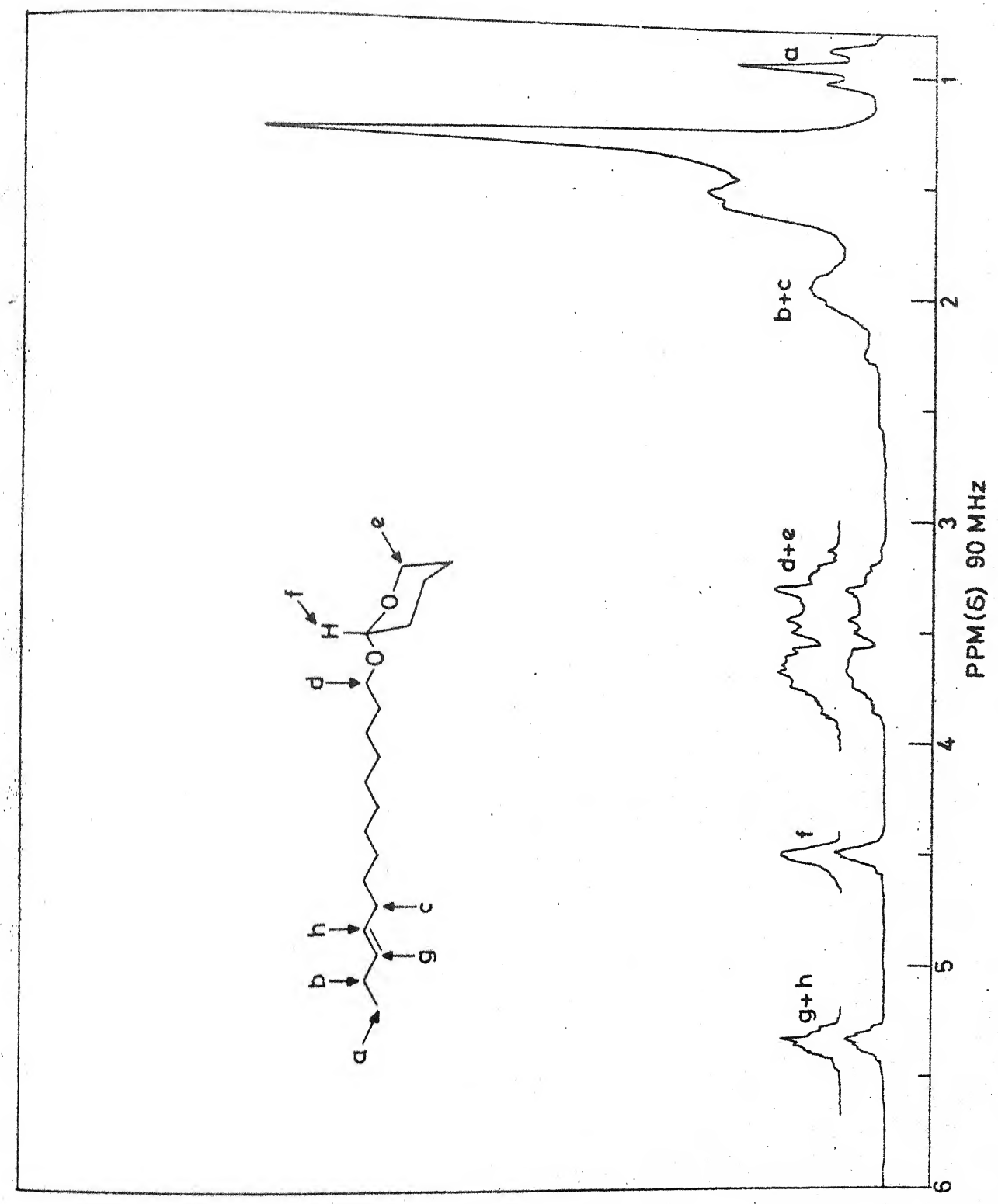

a
b
c
d
e
f
O
H
O
a
b+c
d+e
f
1
2
3
4
5
PPM (δ) 90MHz

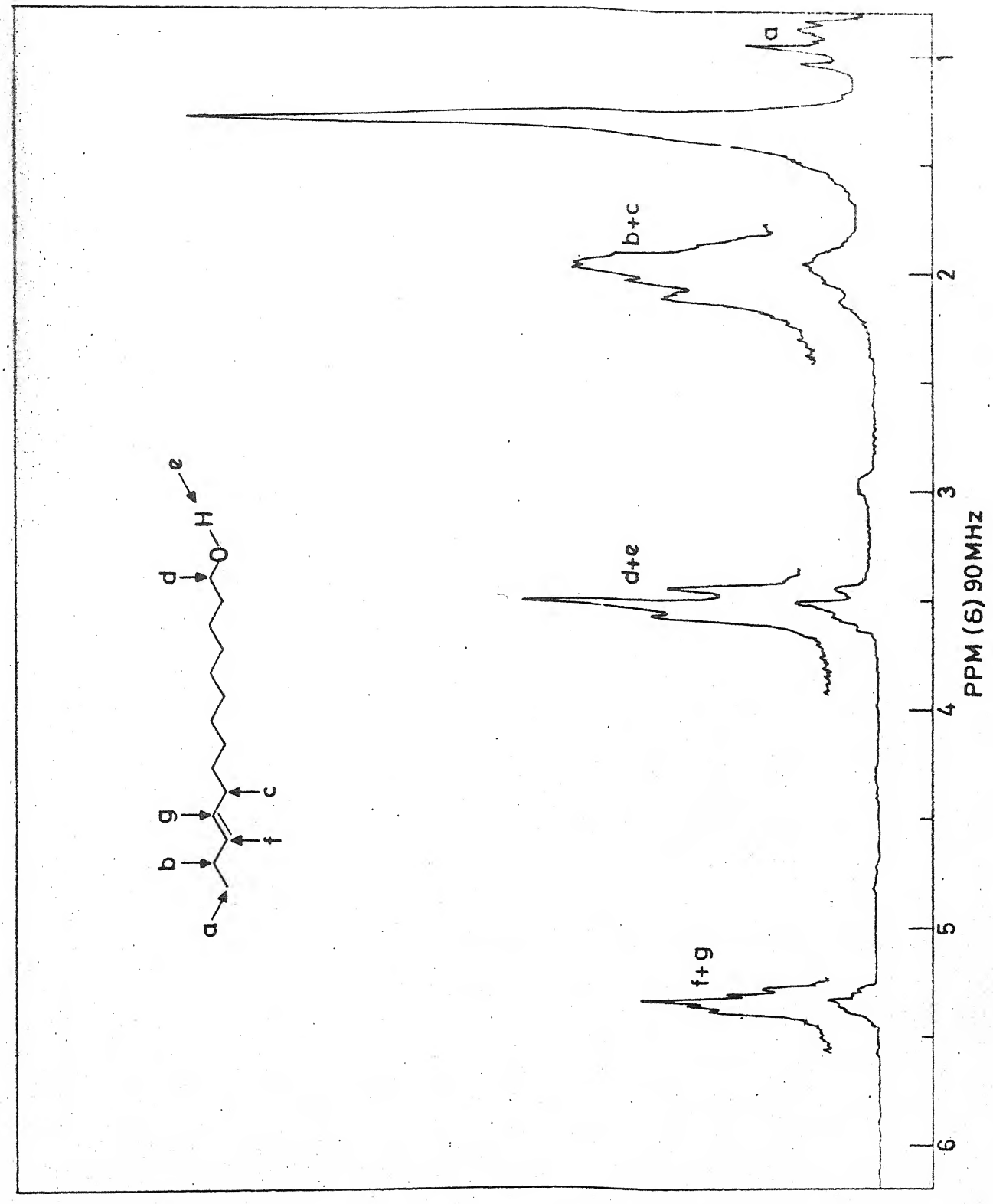

a
b+c
d
e
PPM (δ) 90 MHz
1
2
3
4
5
6
a
b
c
d
e
H
O

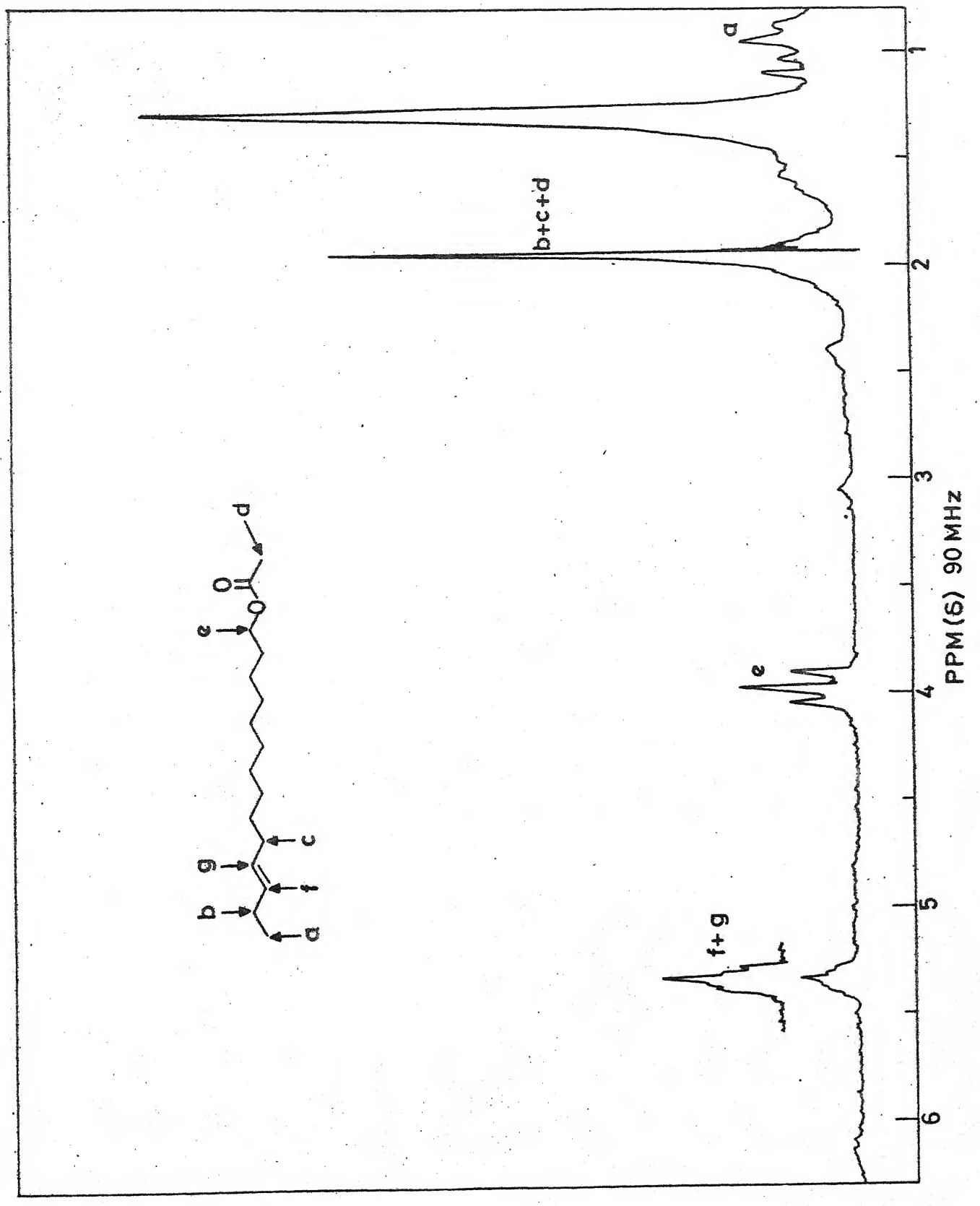

a
b+c
d+e
f+g
1
2
3
4
5
6
PPM (6) 90 MHz
a
b
c
H
H
f
g
O
H
d
e

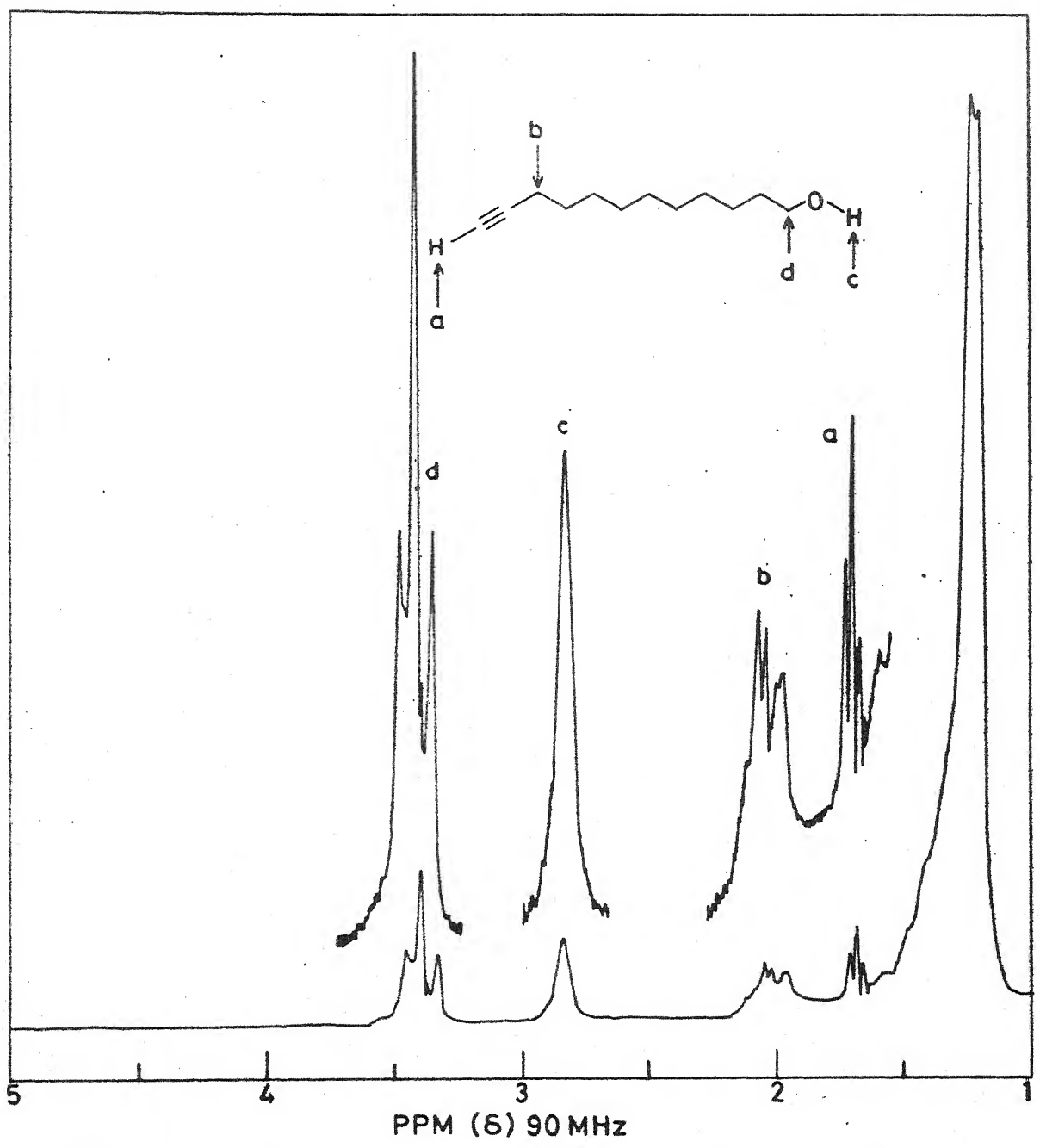

a
b
c+d
e
1
2
3
4
PPM (δ) 90 MHz
a
c
e
O
O
b
d

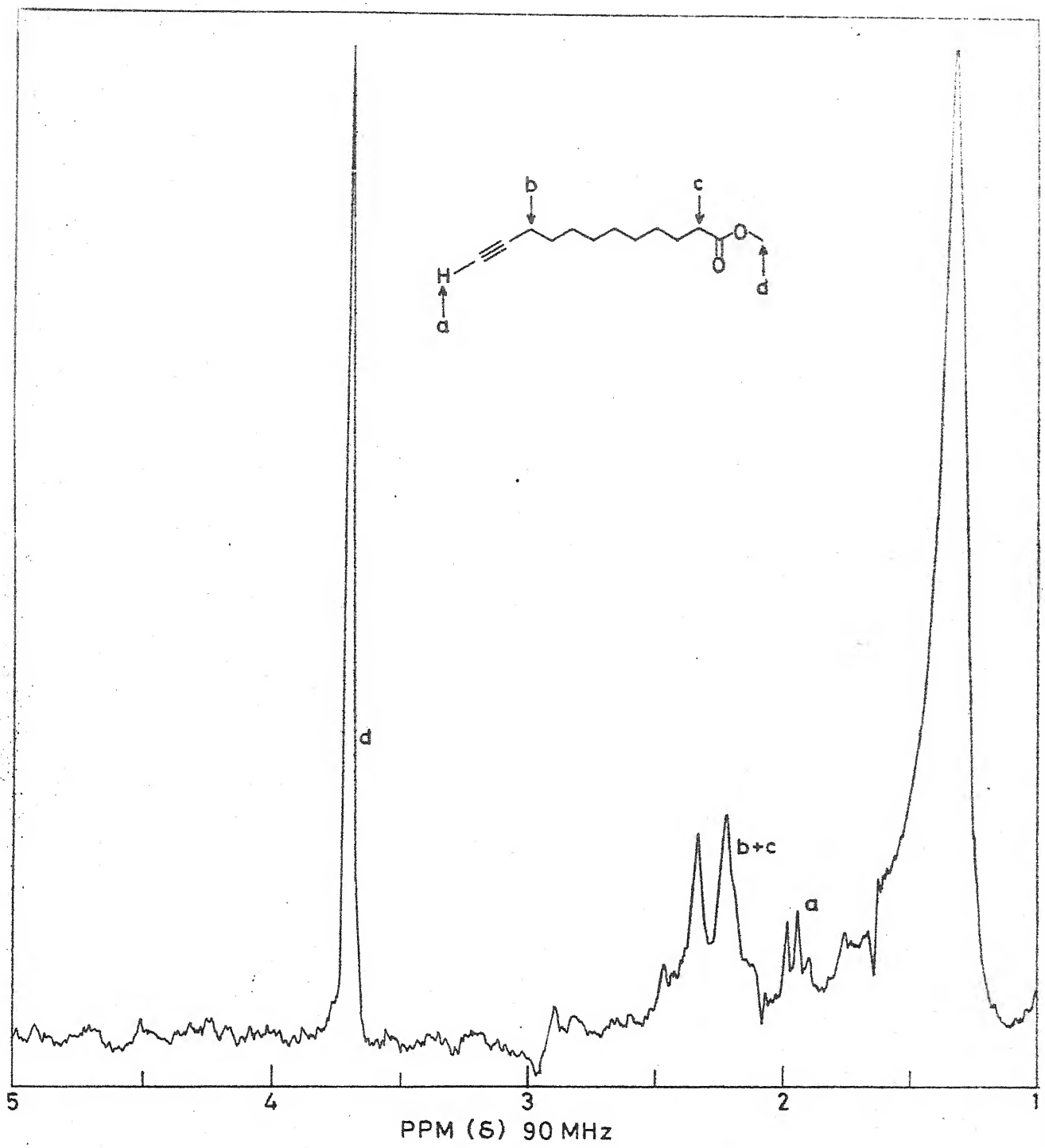

a
b+c+d
e
f+g
1
2
3
4
5
6
PPM(δ) 90 MHz
d
O
O
e
c
H
g
H
f
b
a

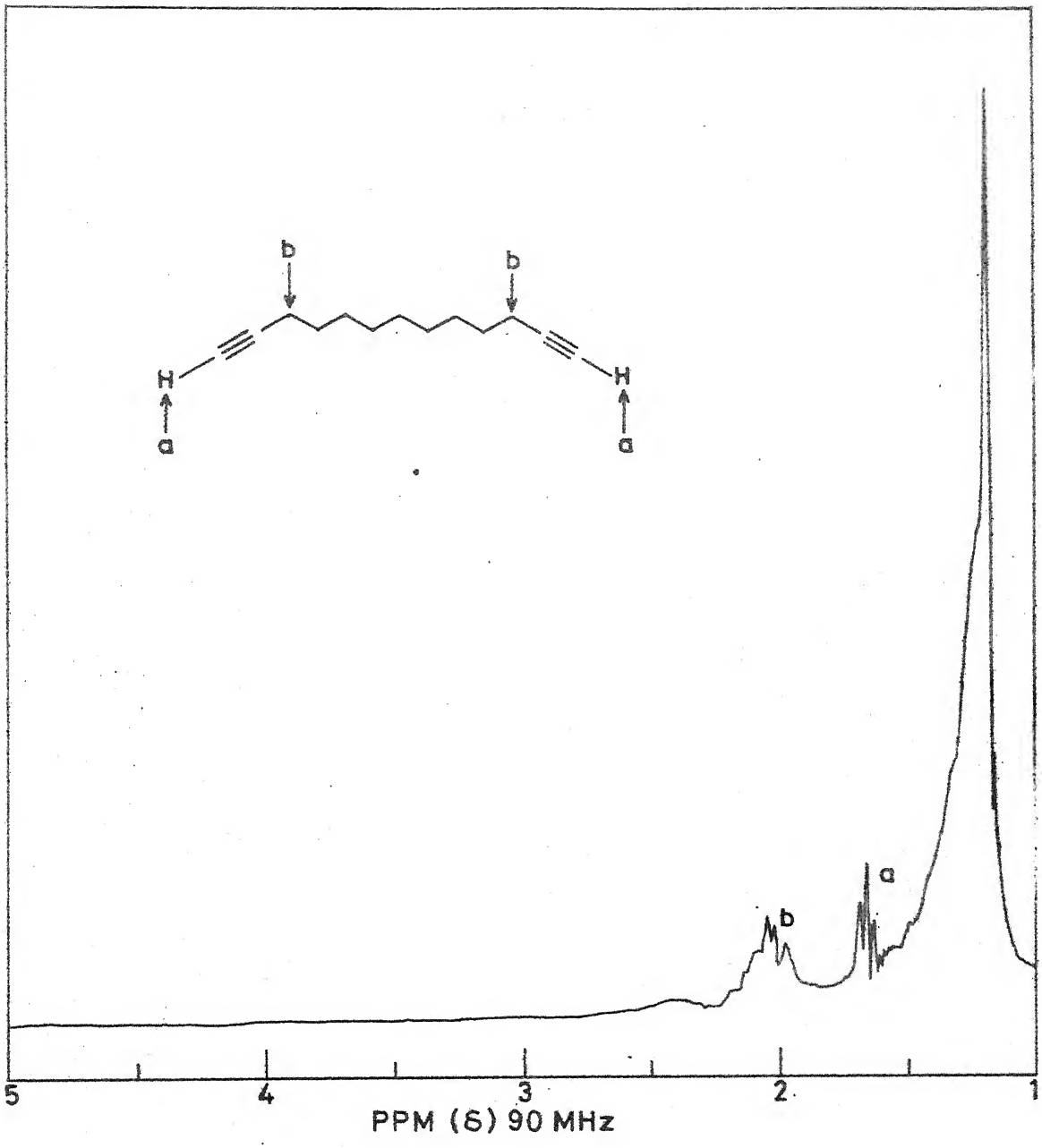

a
b+c
d+e
f
g+h
1
2
3
4
5
6
PPM(δ) 90 MHz
a
b
h
g
c
d
O
f
H
O
e

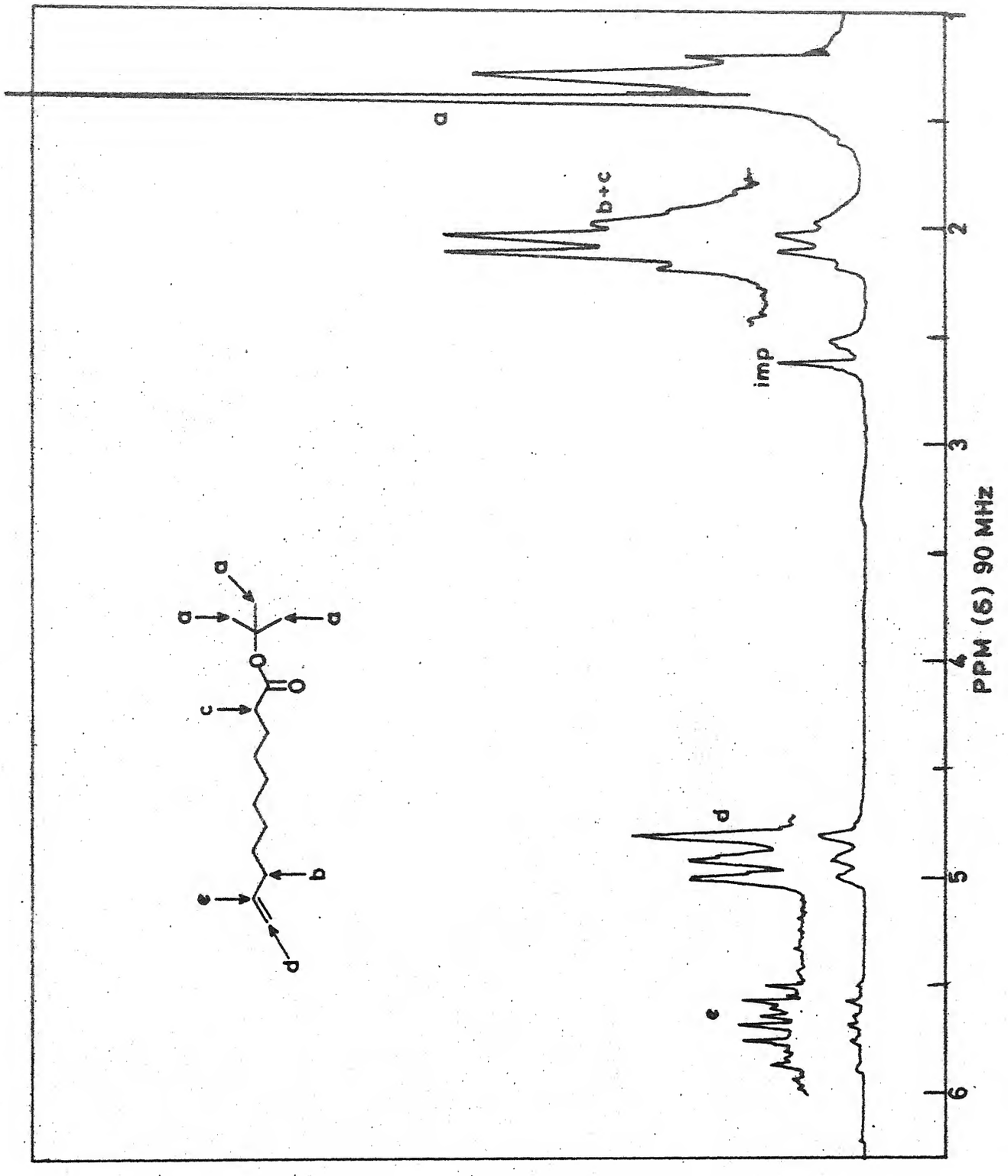

a
b+c
d+e
f+g
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
f
g
H
O

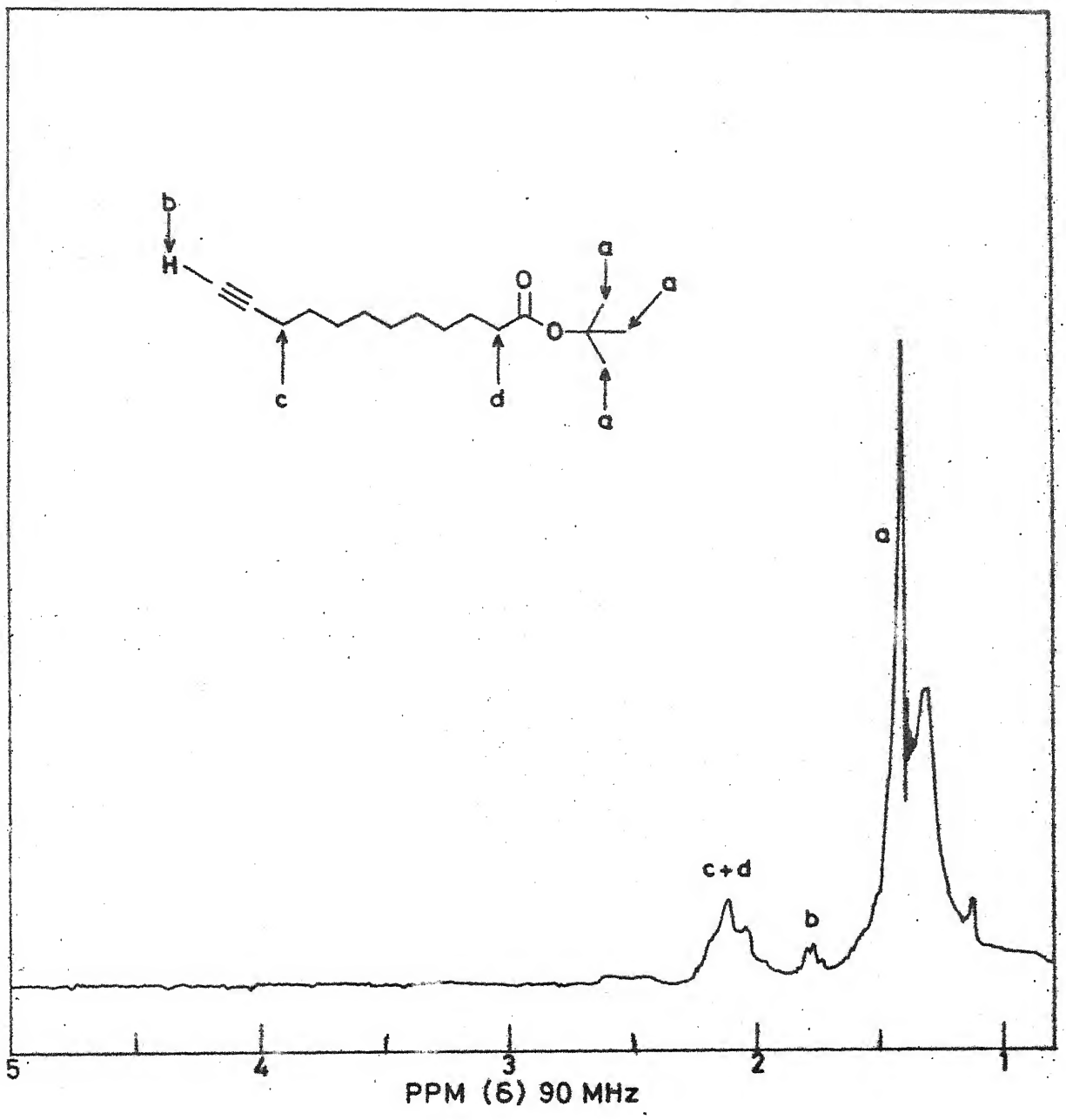

a
b+c+d
e
f+g
1
2
3
4
5
6
PPM(δ) 90 MHz
d
e
O
O
b
g
f
c
a

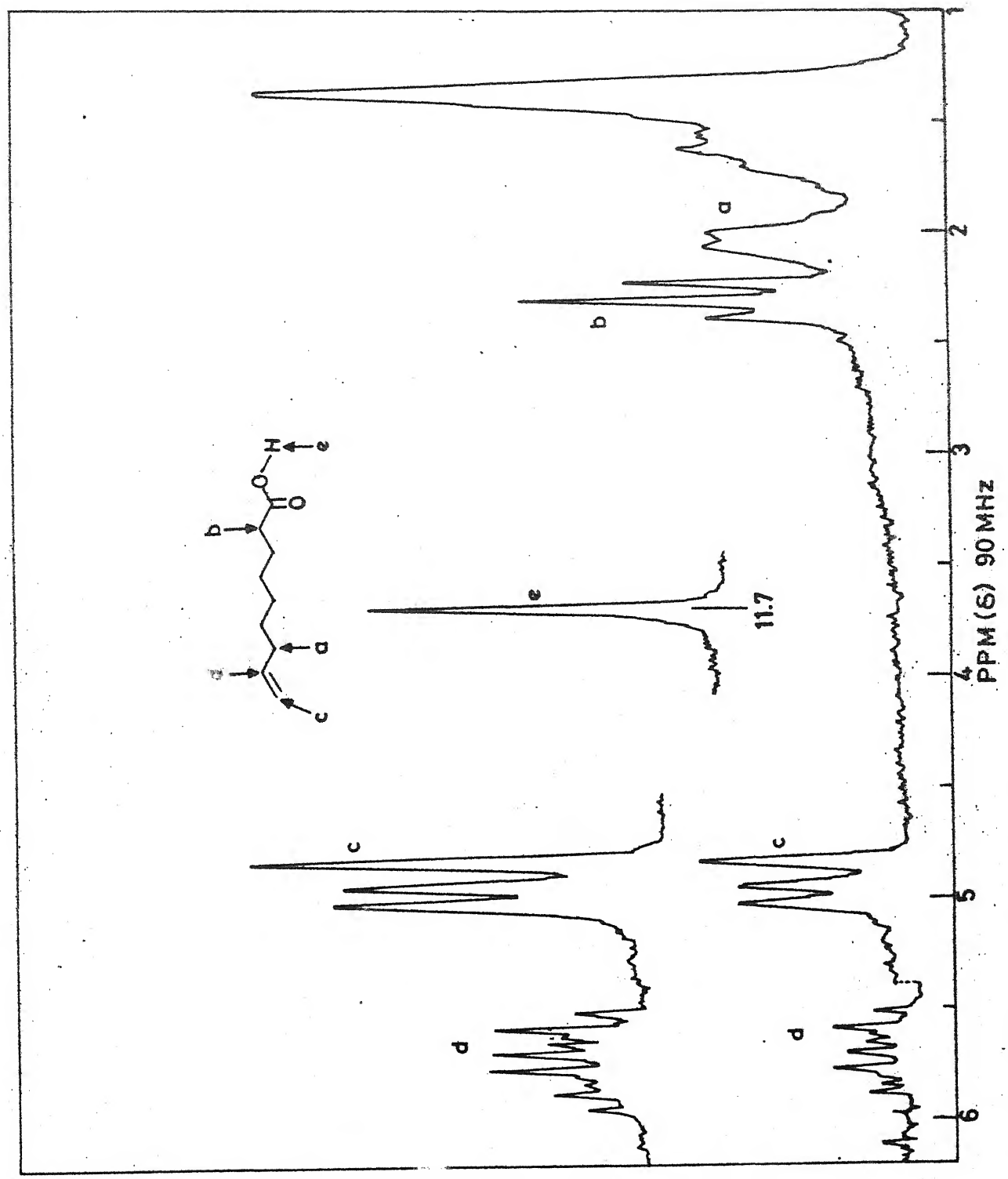

b
H
a
d
O
H
c
d
c
a
b
5
4
3
2
1
PPM (δ) 90 MHz

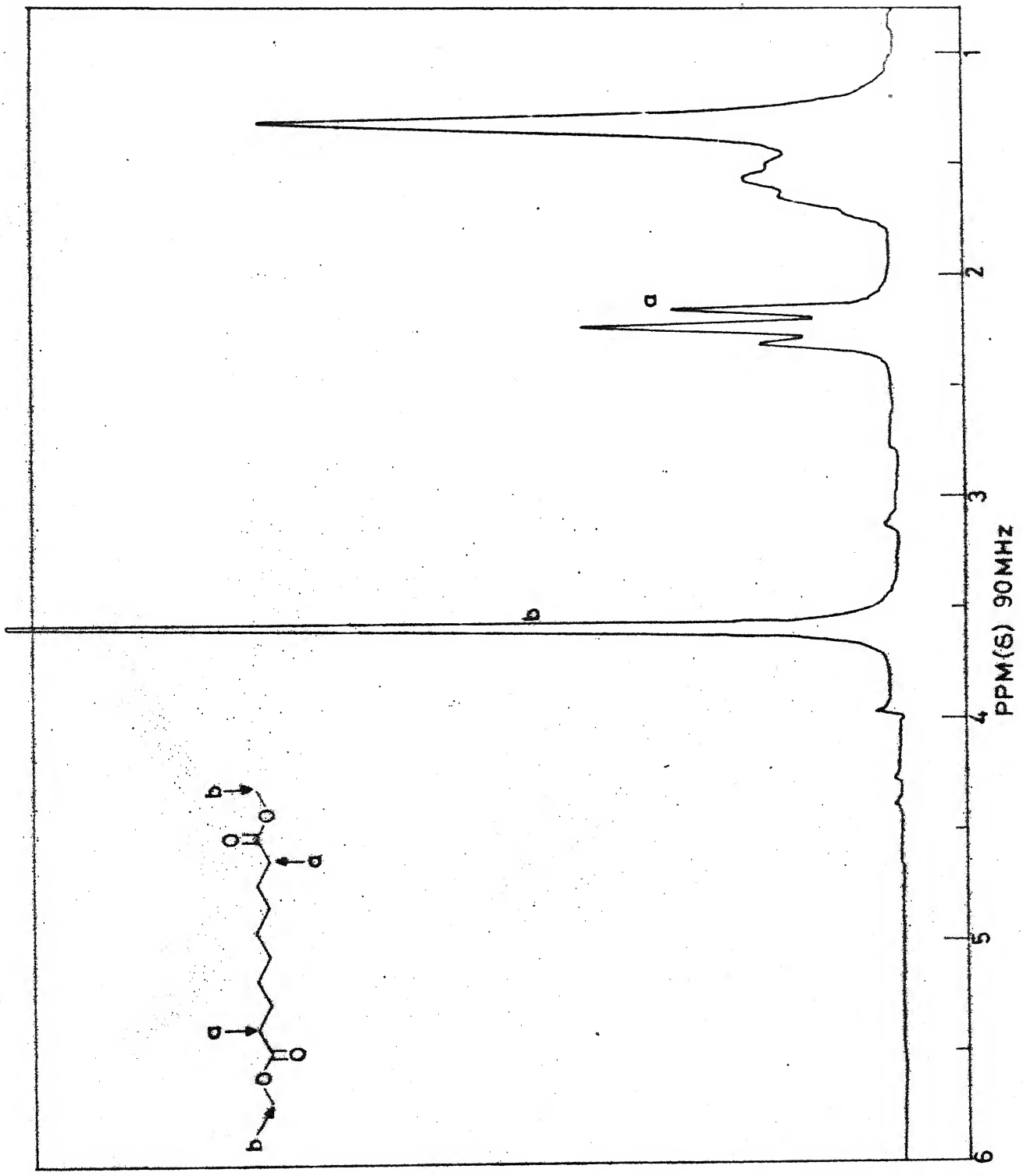

b
c
H
a
O
O
d
d
b+c
a
5
4
3
2
1
PPM (δ) 90 MHz

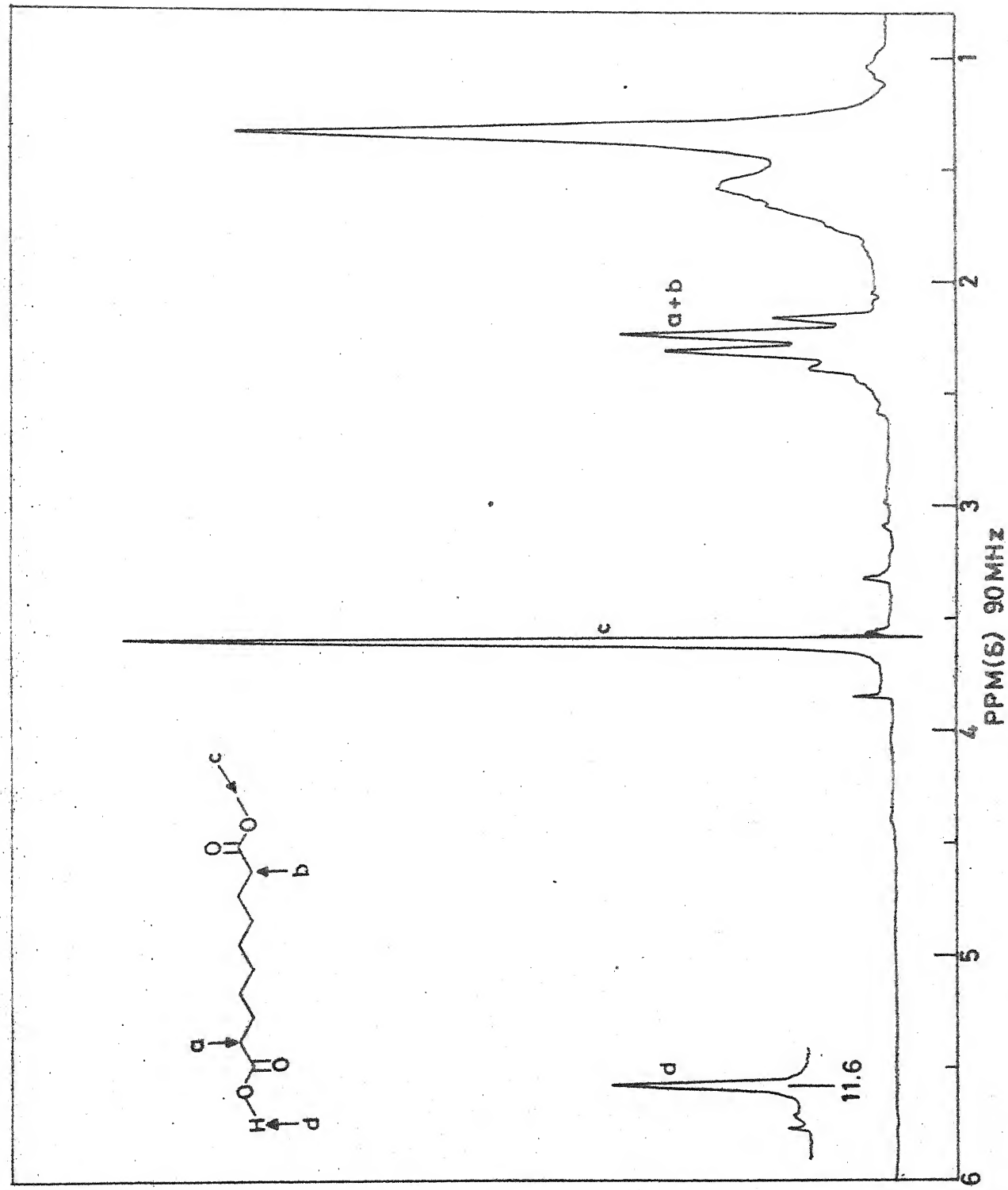

b
b
H
a
H
a
a
b
5
4
3
2
1
PPM (δ) 90 MHz

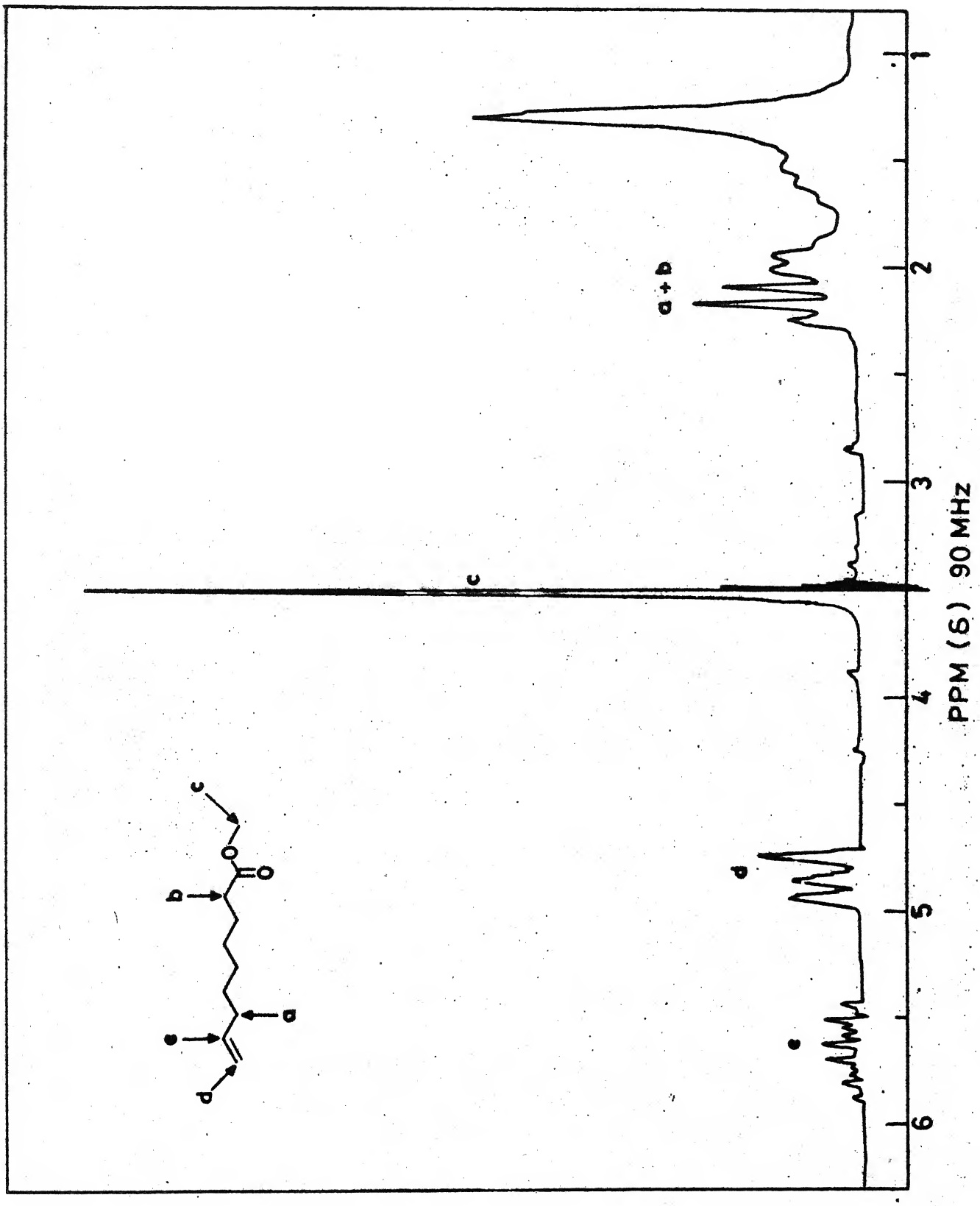

a
b+c
imp
d
e
1
2
3
4
5
6
PPM (δ) 90 MHz
a
a
a
O
O
c
b
e
d

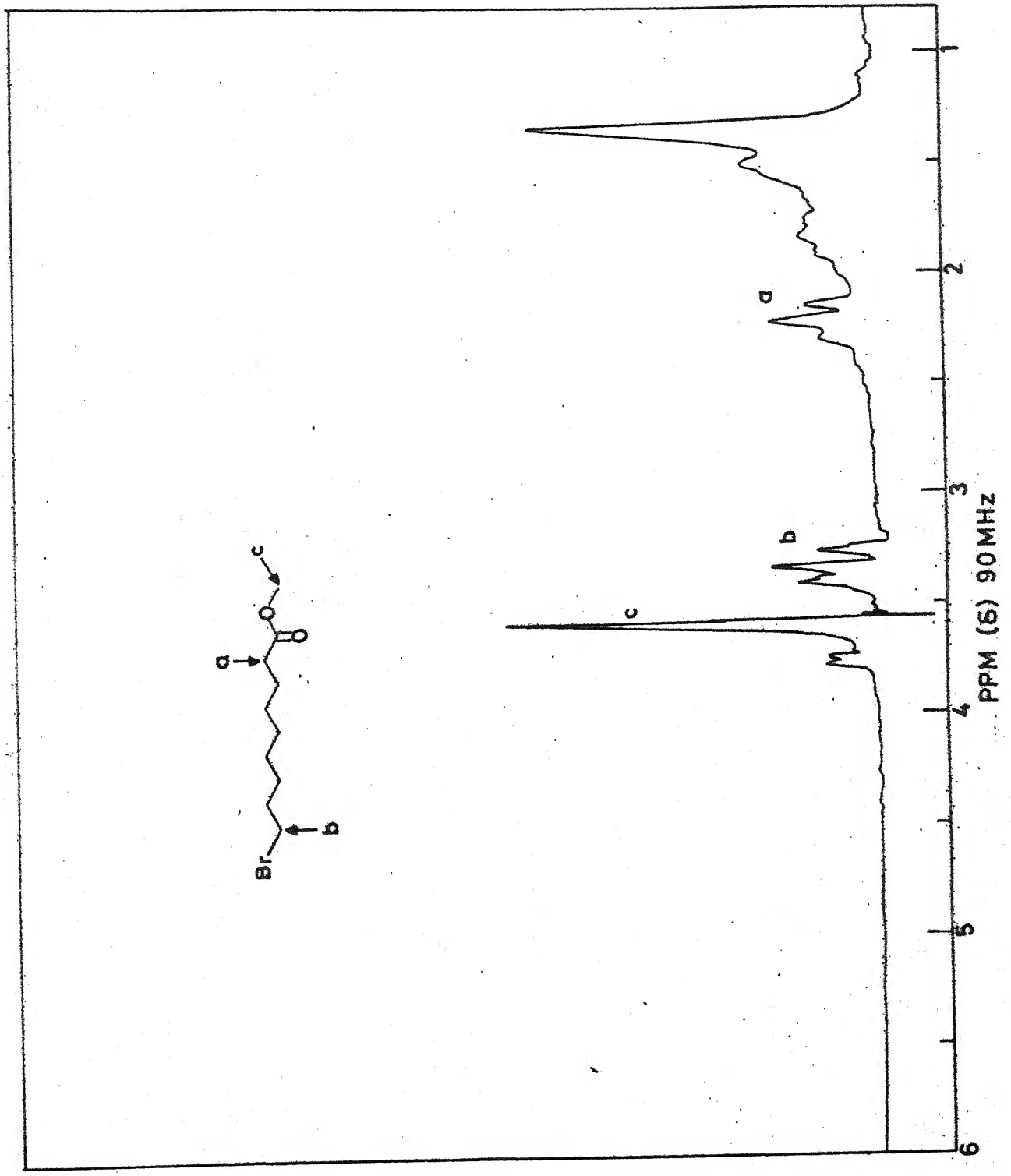

b
H
O
O
a
a
a
c
d
a
c+d
b
5
4
3
2
1
PPM (δ) 90 MHz

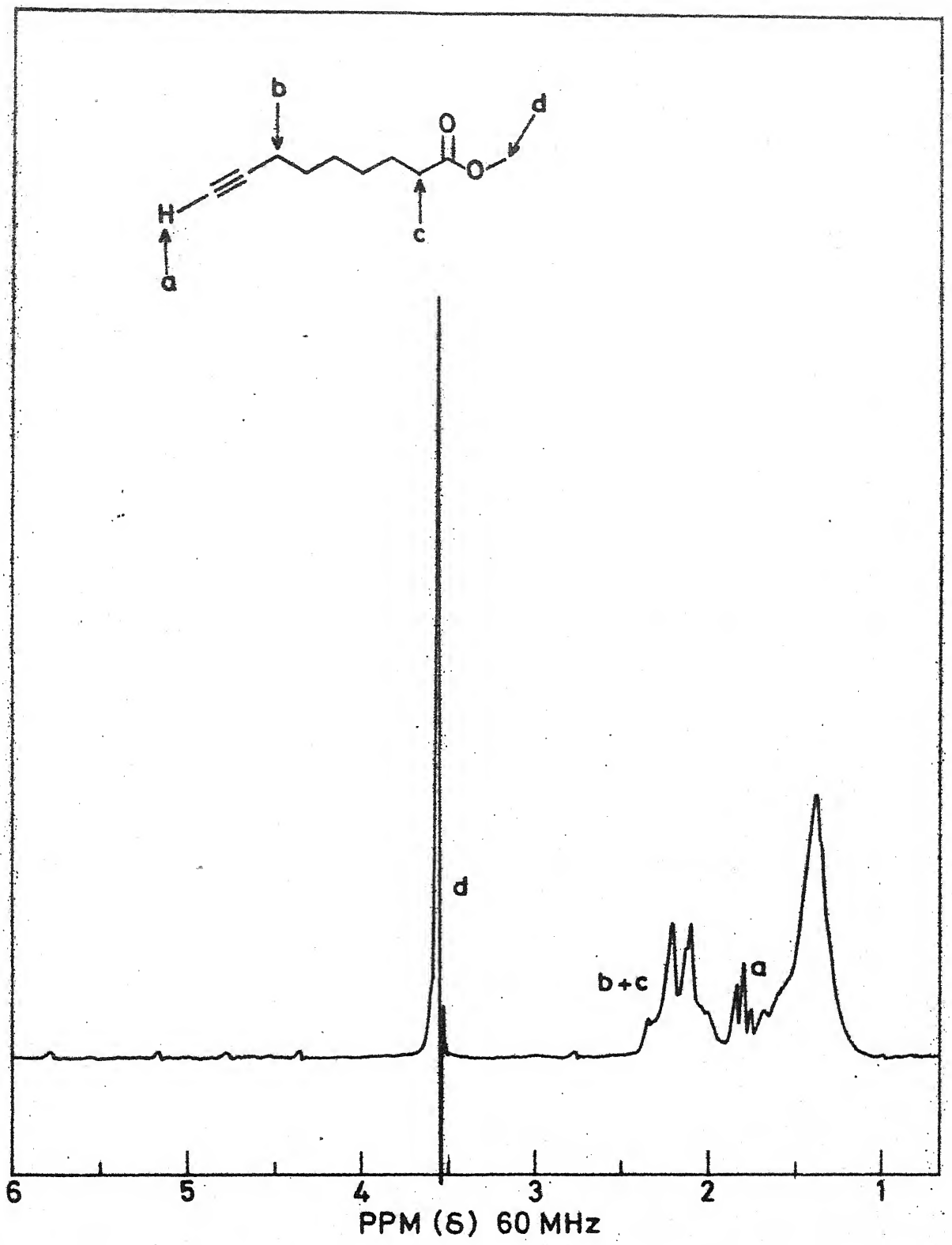

a
b
c
d
e
11.7
PPM (δ) 90 MHz
1
2
3
4
5
6

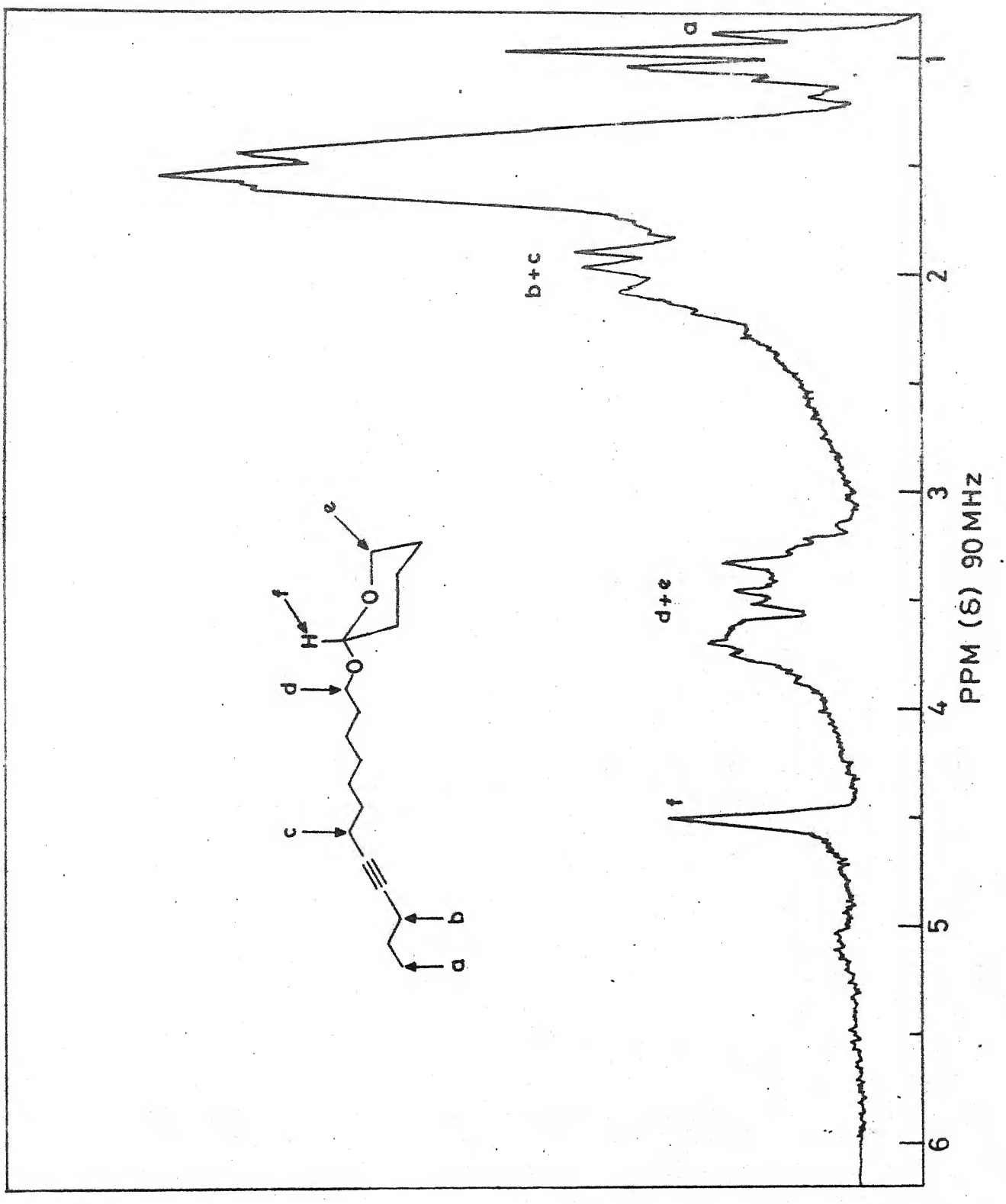

a
b
1
2
3
4
5
6
PPM(δ) 90MHz
b
O
O
a
a
O
O
b

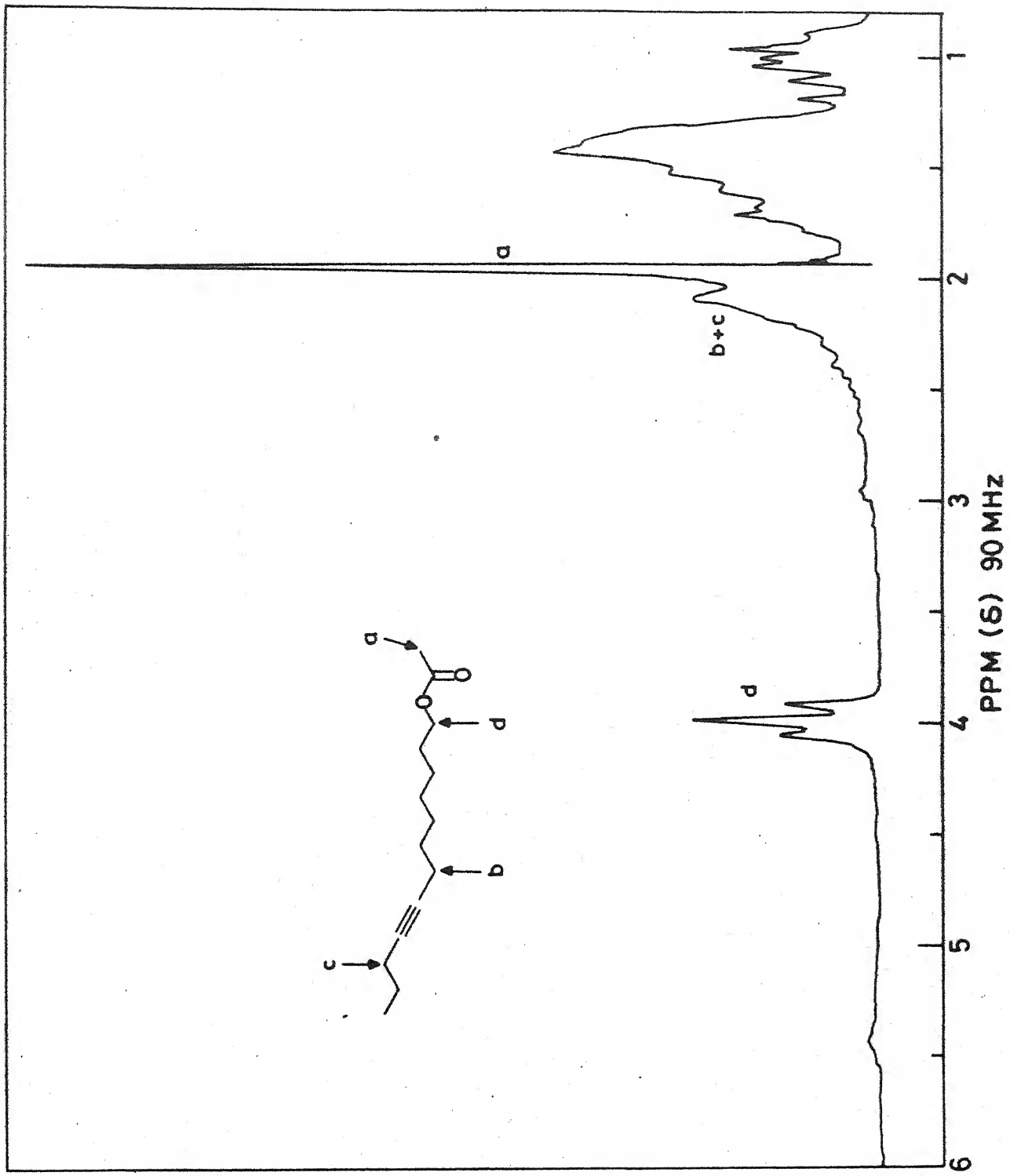

a+b
c
d
11.6
1
2
3
4
5
6
PPM(δ) 90MHz
a
b
c
d

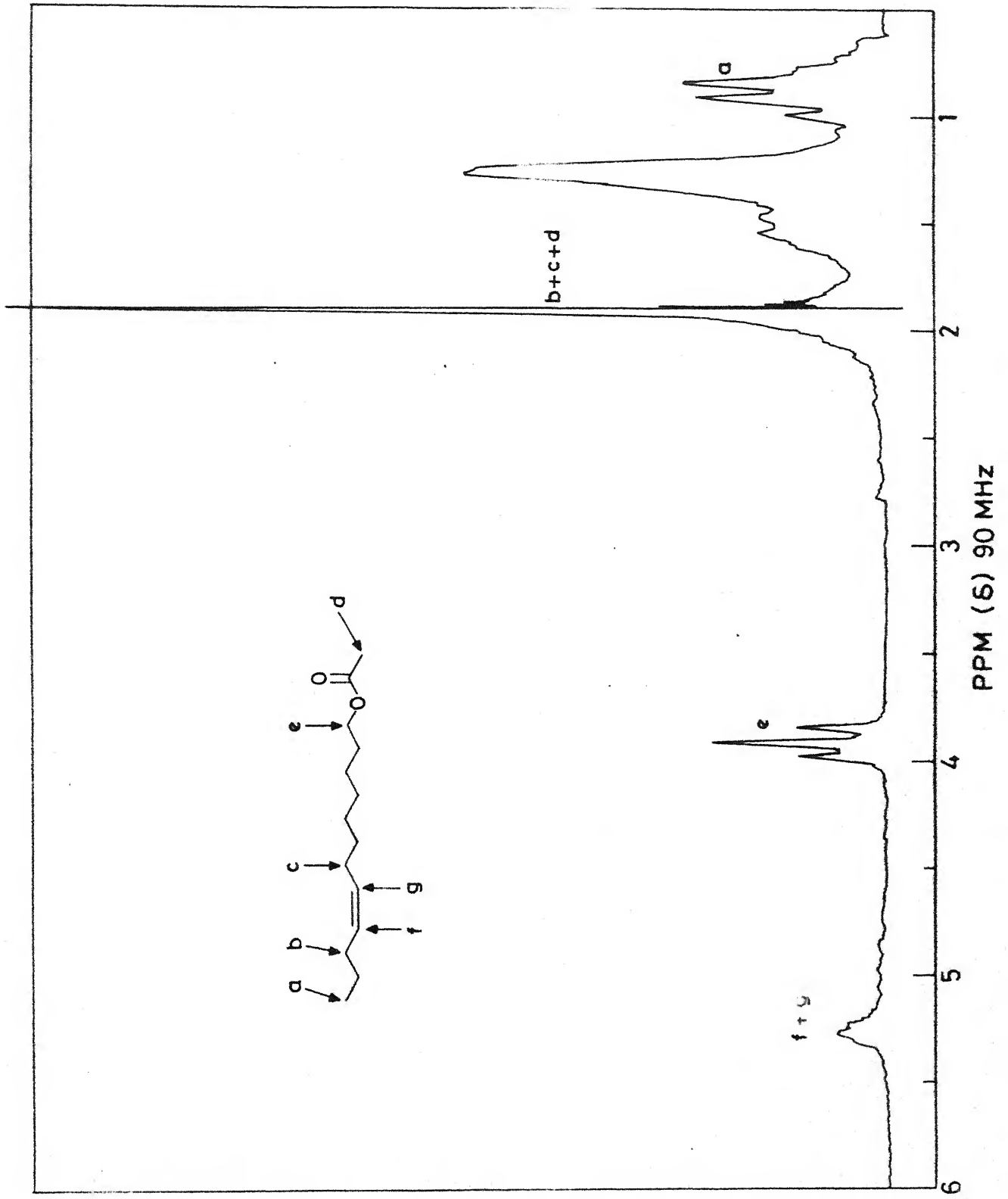

a+b
c
d
e
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
O
O

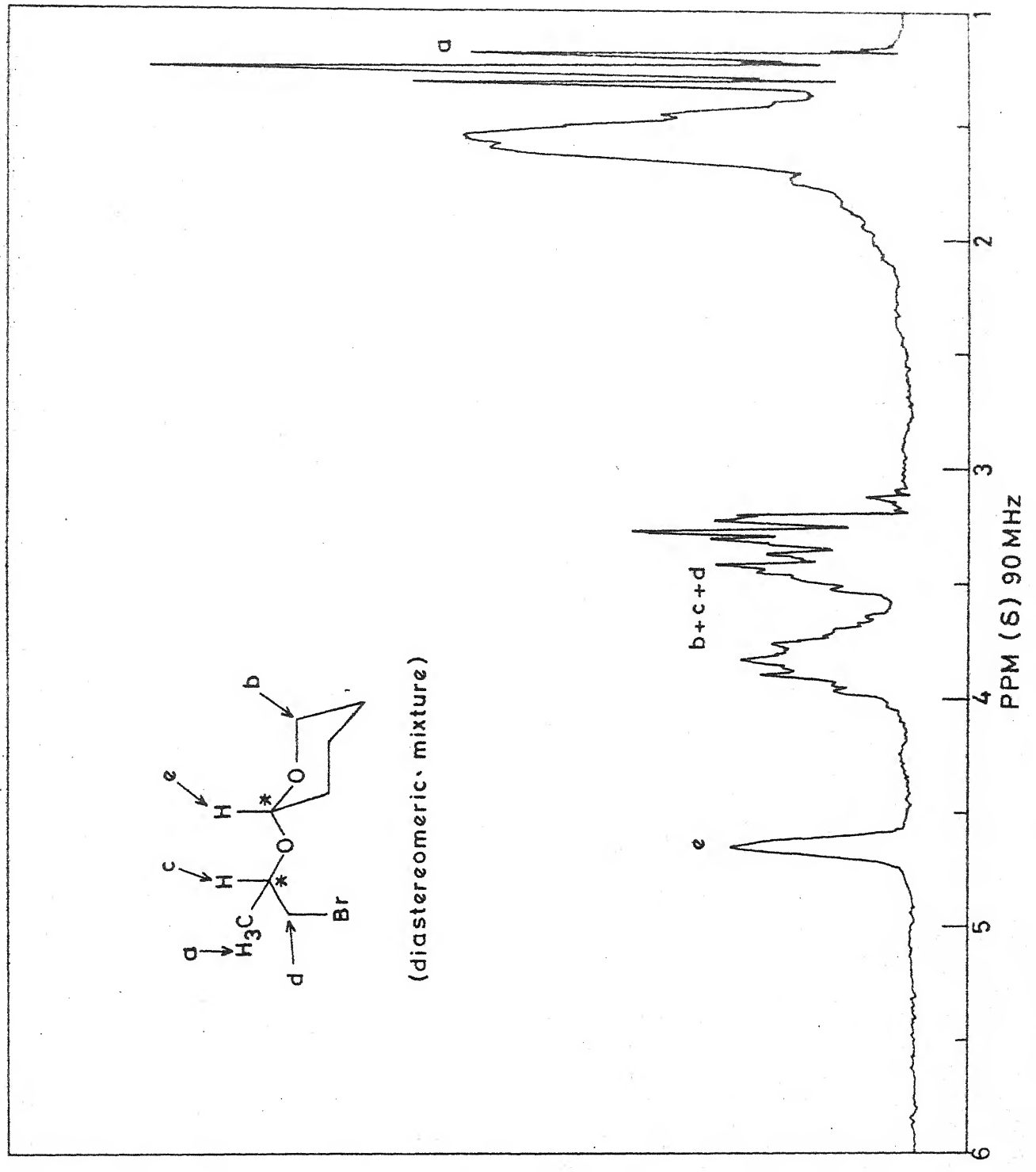

a
b
c
Br
PPM (δ) 90 MHz
1
2
3
4
5
6

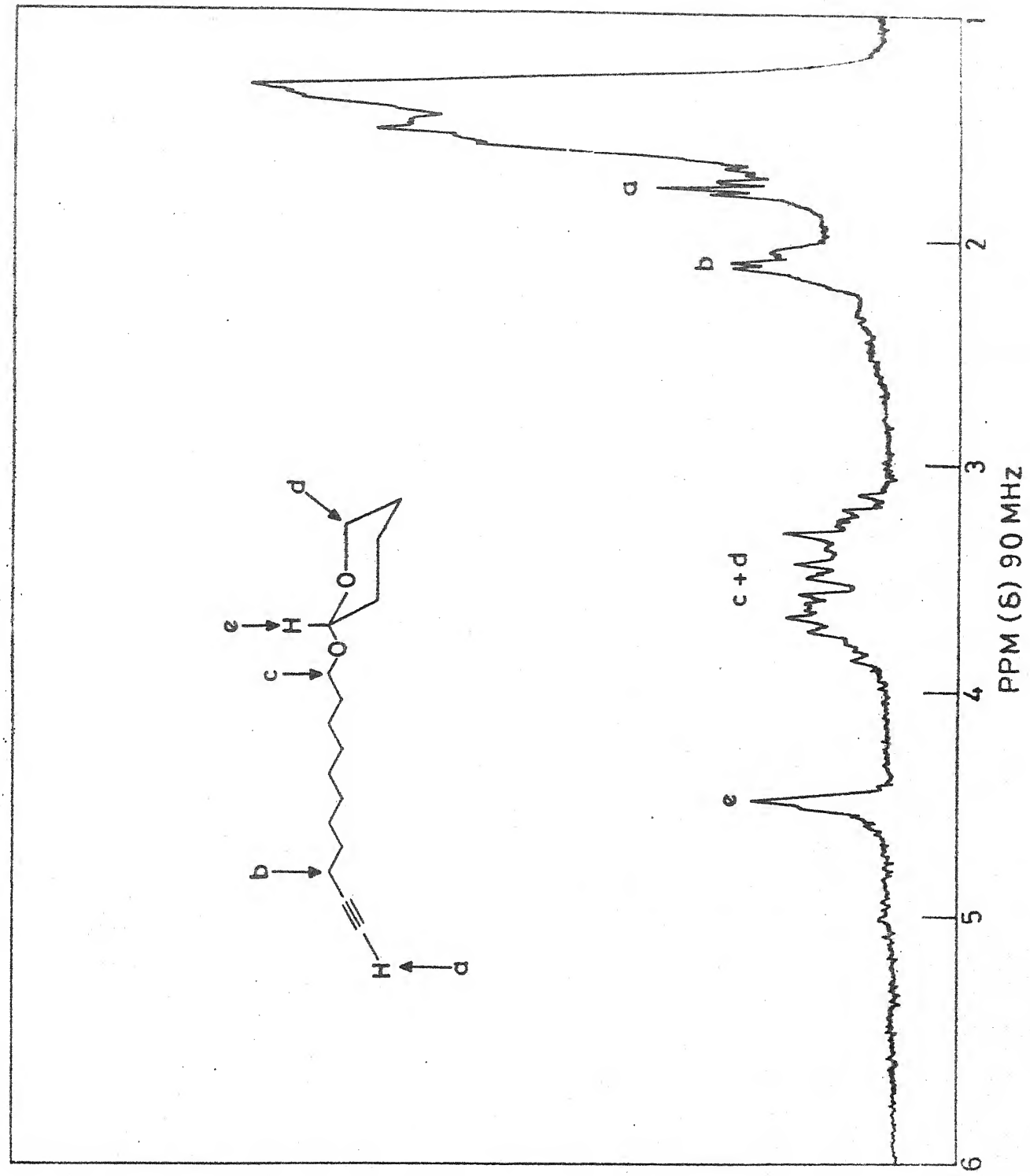

b
d
O
O
H
c
a
d
b+c
a
6
5
4
3
2
1
PPM (δ) 60 MHz

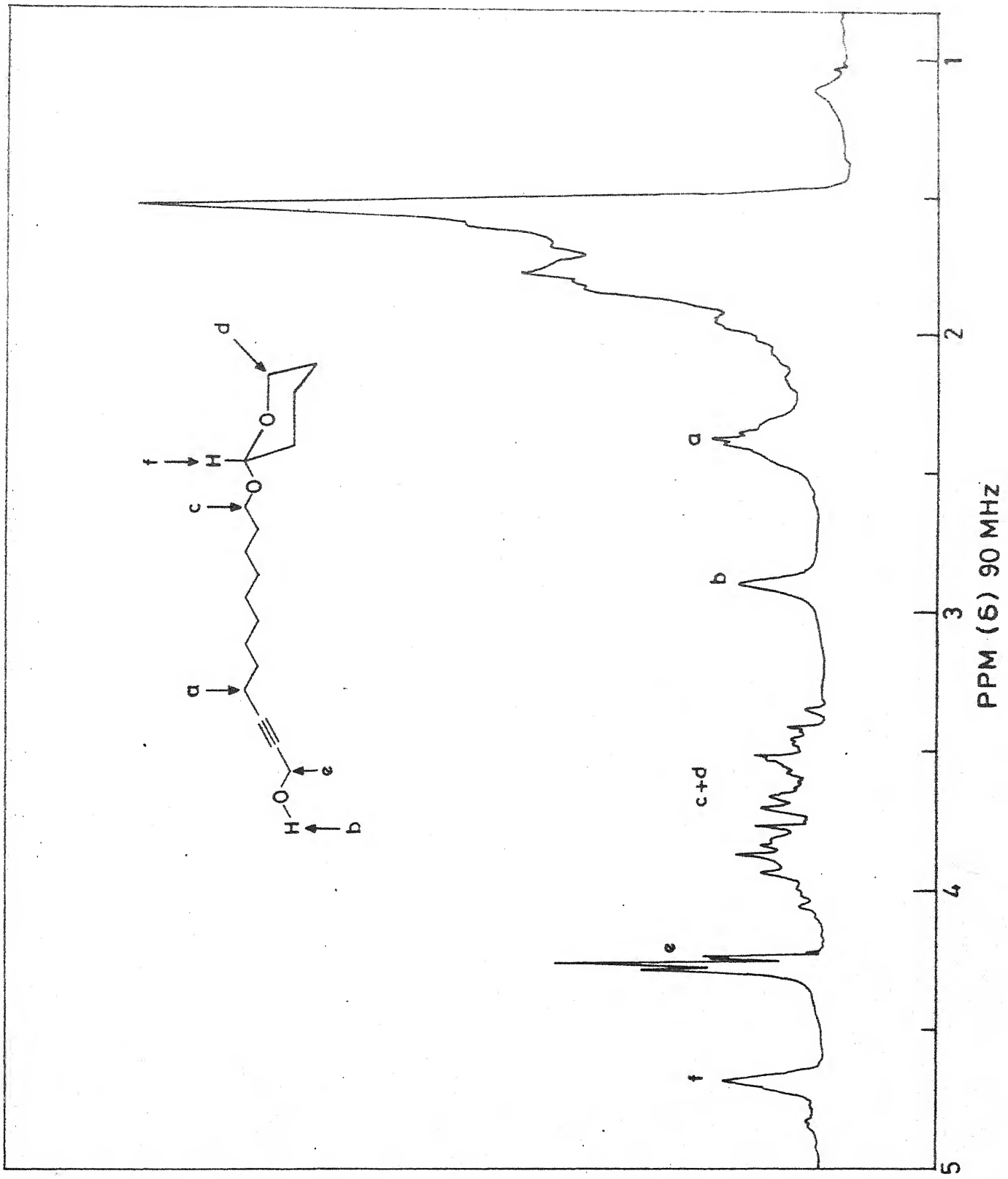

a
b+c
d+e
f
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
f
H
O
O
O

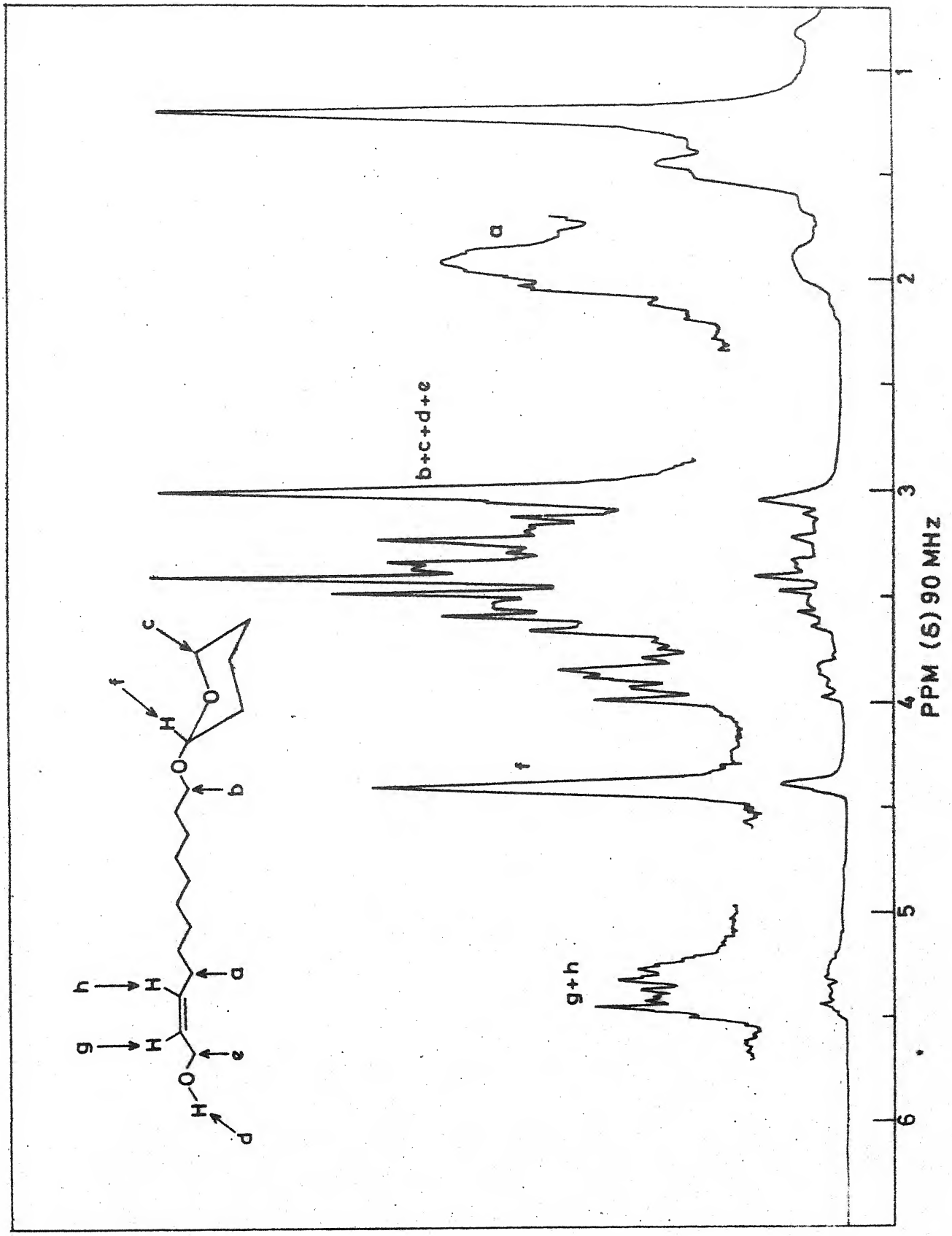

a
b+c
d
1
2
3
4
5
6
PPM (δ) 90 MHz
a
d
b
c

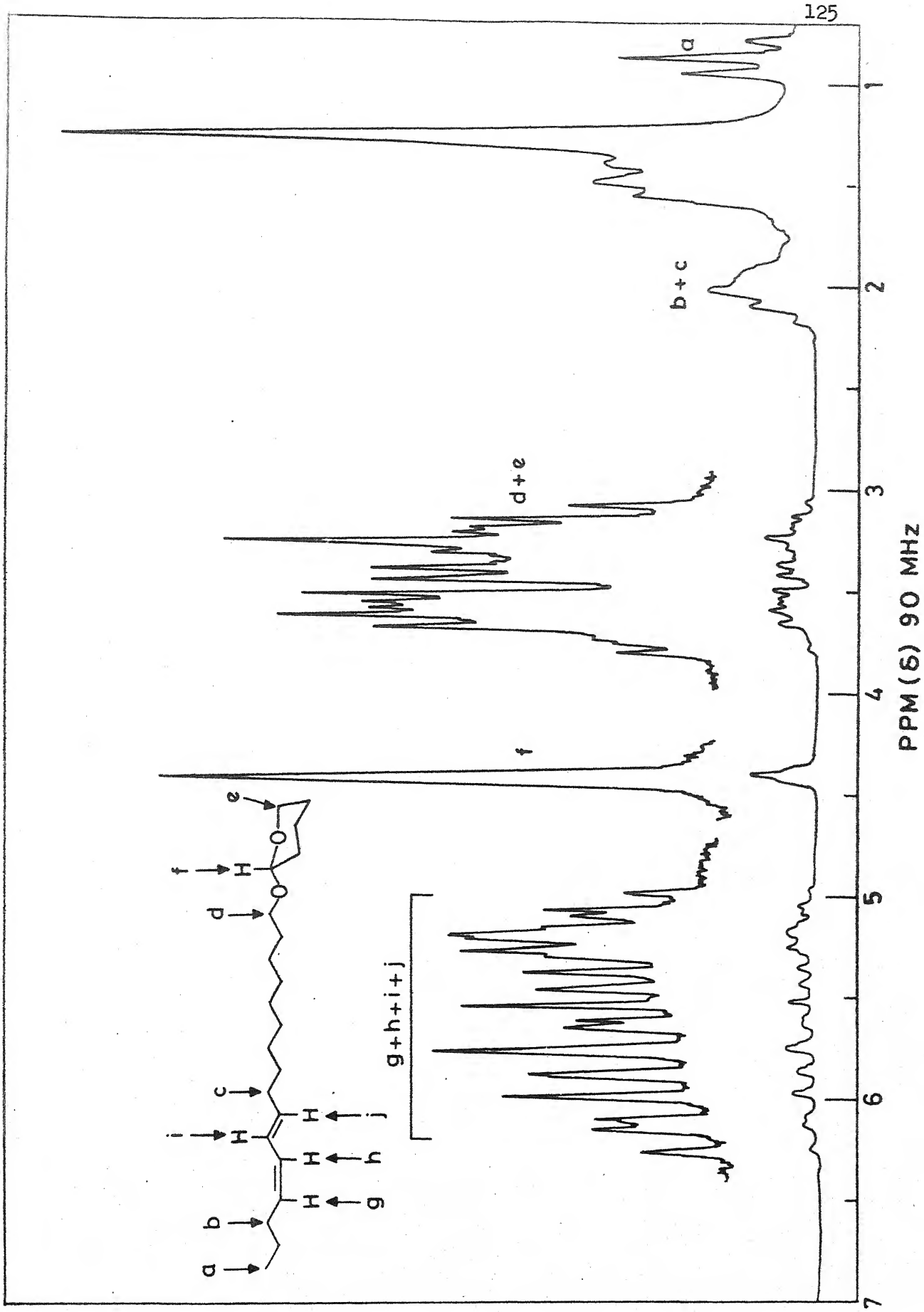

a
b+c+d
e
f+g
PPM (δ) 90 MHz
1
2
3
4
5
6
a b c e d
f g

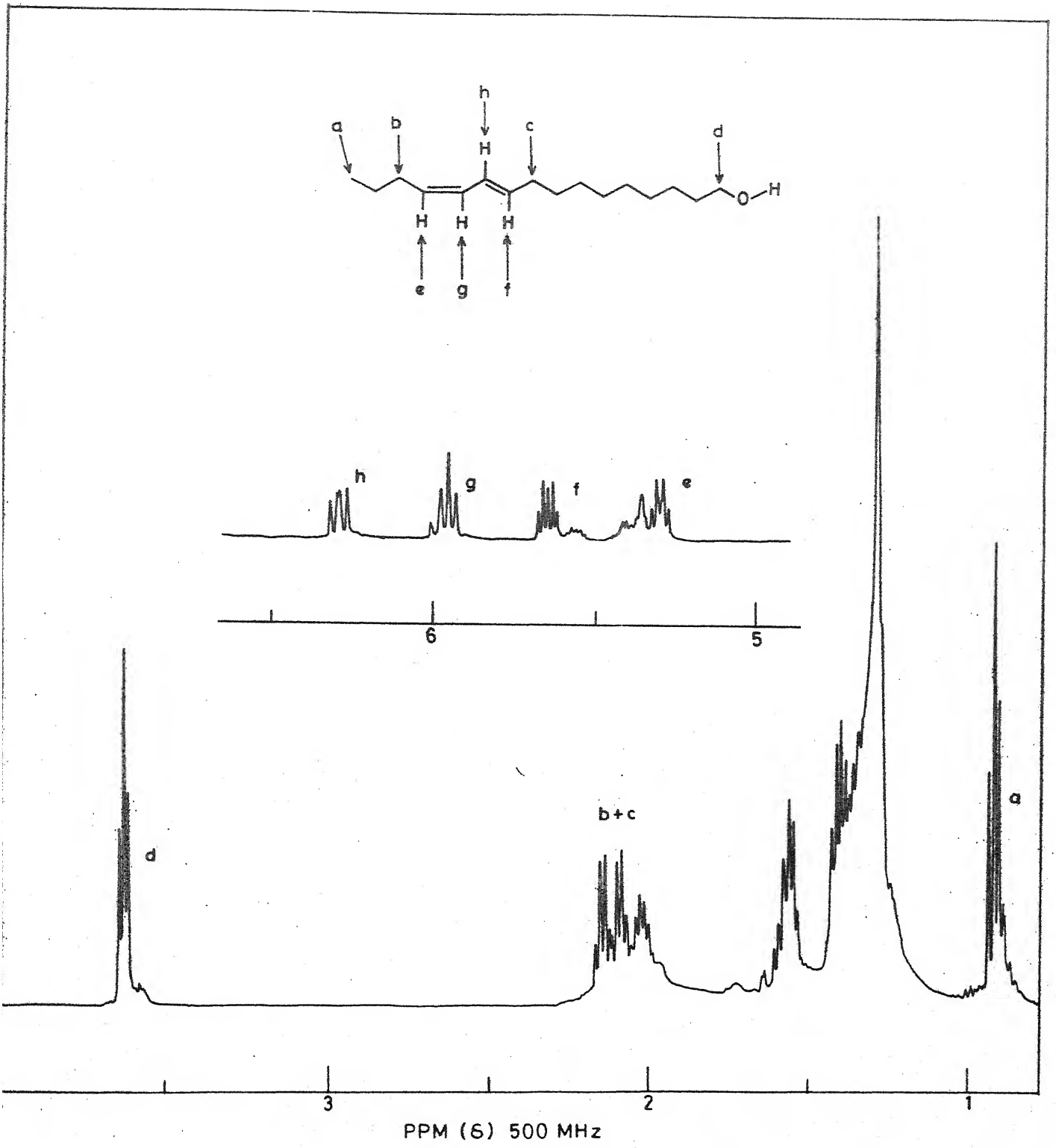

a
b+c+d
e
1
2
3
4
5
6
PPM (δ) 90 MHz
(diastereomeric mixture)
a
b
c
d
e
H
H
H3C
Br
O
O
*
*

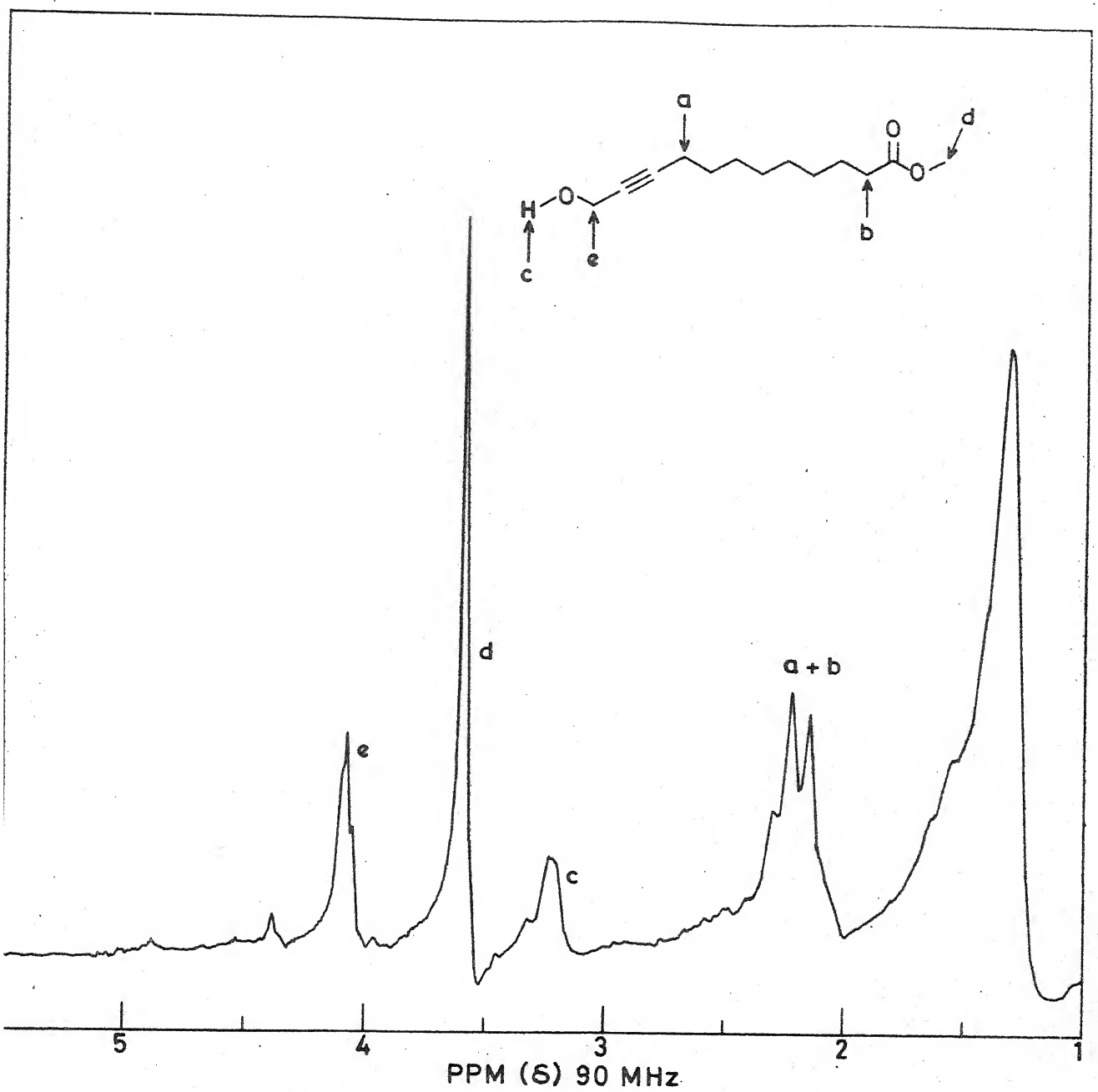

d
e
H
O
O
c
b
H
d
a
b
c+d
e
1
2
3
4
5
6
PPM (δ) 90 MHz

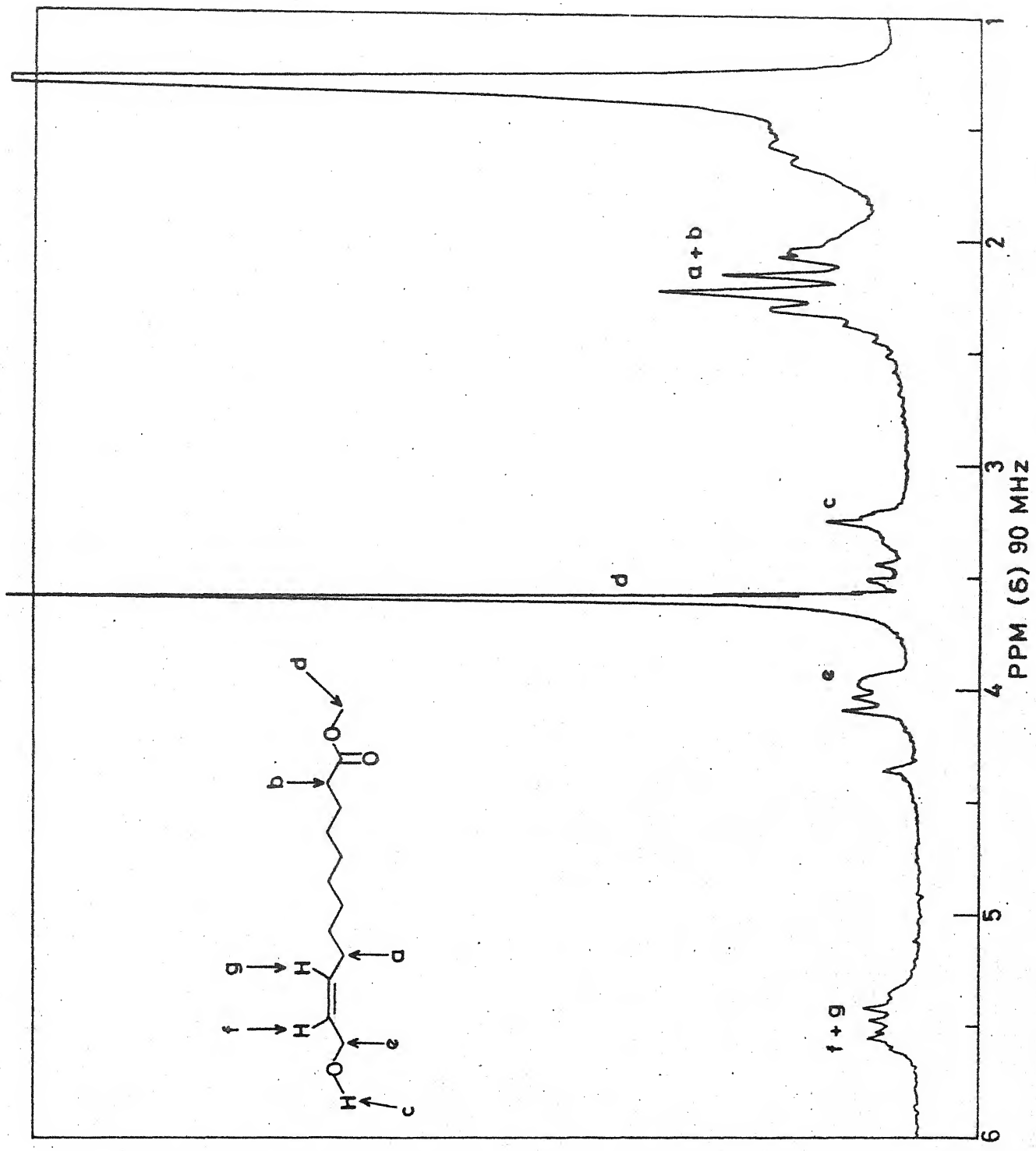

PPM (δ) 90 MHz
1
2
3
4
5
a
b
c+d
e
f
a
b
c
d
e
f
H
O
H

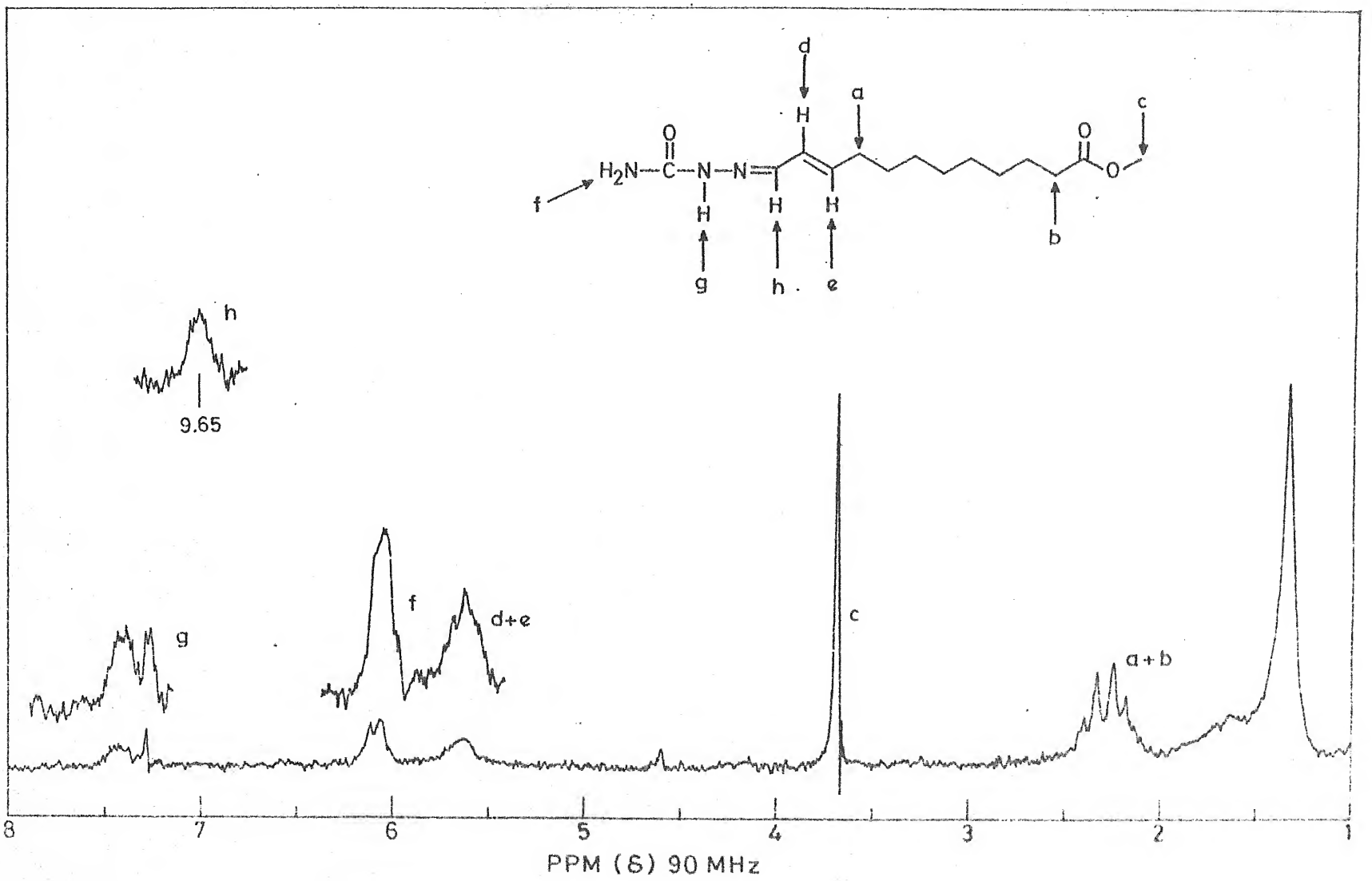

a
b+c+d+e
f
g+h
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
f
g
h
p
H
O


a
b+c
d+e
f
g+h+i+j
PPM (δ) 90 MHz
1
2
3
4
5
6
7
a
b
c
d
e
f
g
h
i
j
H
O


h
a
b
c
d
H
H
H
H
O
H
e
g
f
h
g
f
e
6
5
d
b+c
a
3
2
1
PPM (6) 500 MHz


a
d
O
O
H
O
b
c
e
d
a + b
e
c
5
4
3
2
1
PPM (δ) 90 MHz


a+b
c
d
e
f+g
1
2
3
4
5
6
PPM (δ) 90 MHz
a
b
c
d
e
f
g
H
H
O
O
O


d
a
c
f
b
g
h
e
h
9.65
g
f
d+e
c
a+b
8
7
6
5
4
3
2
1
PPM (δ) 90 MHz

E. EXPERIMENTAL

Bps are uncorrected. IR spectra were recorded on Perkin Elmer Model 580 spectrophotometer as neat liquids. NMR spectra were obtained on ~ 10-15% solutions in CCl_4 or $CDCl_3$ on R-32 and EM 390 spectrometers. The chemical shifts are reported in ppm downfield from internal TMS at 0.00 as internal standard. Elemental analyses were carried out in Coleman automatic C,H analysers, silica gel G (acme) was used for tlc and column chromatography was done on silica gel (acme, 100-200 mesh) columns. Reactions were monitored, wherever possible, by tlc. GC analysis was done on 1.8m x 2mm i.d. 5% SE 30/0.5% Carbowax 20M/Chromosorb W HP, 1.8m x 2mm i.d. 1.5% Carbowax 20M on Chromosorb G AW DMCS, 100-120 mesh, and 1.8m x 2mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene on Gas Chrom Q columns.

I. Trans-esterification of castor oil (1; R=glyceride): Preparation of methyl ricinoleate (1; R= -Me)

A solution of castor oil (932 g, 1 mol) in MeOH (3.5 l), containing *in situ* generated NaOMe [from Na (1.0 g, 0.043 mol)], was refluxed for 1 hr, solvents evaporated, the residue shaken with 50% aqueous MeOH (300 ml), the upper layer separated, dried ($MgSO_4$) and distilled to give 795.6 g (85%) of methyl ricinoleate (1, R=Me), bp 128-130°/0.02 torr.

Anal. Calcd. for $C_{19}H_{36}O_3$ (Mol. Wt. 312)
C, 73.07; H, 11.53
Found C, 73.18; H, 11.48%

ir: ν_{max}(neat)(cm^{-1}): 3440 (hydroxyl), 1742 (ester).

nmr: $\delta_{(CDCl_3)}$: 3.65 (s, 3H, $-COOCH_3$), 5.45 (m, 2H, -CH=CH-).

II. $\pi^2s + \sigma^2s + \sigma^2s$ Fragmentation of methyl ricinoleate (1, R=Me): Isolation of methyl undec 10-enoate (2) and n-heptaldehyde (3)

Under a set-up for distillation, methyl ricinoleate (100g), evenly supported on clean sand (50g), was pyrolysed with a Bunsen burner of luminous flame for 0.75 hr, during which 87.0g of a light green distillate was collected. The small amount of water that came over was separated and the residue on distillation gave heptaldehyde (3) (11.3g, 77%) (152°/760 torr), methyl undec 10-enoate (2) (12.5g, 49%), bp 80-81°/0.9 torr and unchanged methyl ricinoleate (60.0g).

Anal. Calcd. for $C_{12}H_{22}O_2$ (Mol. Wt. 198)

C, 72.72; H, 11.1

Found C, 72.9 ; H, 11.24%

ir: ν_{max}(neat)(cm^{-1}): 1742 (ester), 1640 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.68 (s, 3H, $-COOC\underline{H}_3$), 4.98 (m, 2H, $C\underline{H}_2=CH-$), 5.78 (m, 1H, $CH_2=C\underline{H}-$).

III. Lithium Aluminium hydride reduction of 2: Preparation of 1-hydroxy undec 10-ene (4)

A solution of 2 (5.5g, 0.028 mol) in dry ether (50 ml) was added, in drops, to a well stirred suspension of LAH (2.0g, 0.052 mol) in dry ether (100 ml). The mixture was left stirred till reaction was complete (tlc, ~2 hr), excess reagent destroyed by cautious addition of water, acidified with ice-cold 2N H_2SO_4, diluted with ether, the organic layer washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$), solvents evaporated and the residue distilled to give 4.5g (95.3%) of 4, bp 76-80°/0.05 torr.

Anal. Calcd. for $C_{11}H_{22}O$ (Mol. Wt. 170)

C, 77.65; H, 12.94

Found C, 77.56; H, 12.94%

ir: ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 1645 (double bond).

IV. Reaction of alcohol 4 with DHP in presence of PPTS: Preparation of 1-tetrahydropyranyloxy undec 10-ene (5)

Pyridinium p-toluenesulfonate (PPTS) was prepared by cautious addition of p-toluene sulfonic acid monohydrate (5.7g, 30 mmol) to stirred pyridine (12 ml, 150 mmol), followed by, after additional 0.5 hr stirring at RT, evaporation of solvents *in vacuo* at 60° and crystallisation from acetone; yield 6.8g (90%), mp 120°.

A solution of alcohol 4 (4.0g, 0.024 mol), 5,6-dihydropyran (3.024g, 0.036 mol) and PPTS (0.62g, 0.0024 mol) in CH_2Cl_2 (70 ml) was left stirred, at RT, for 4 hr, diluted with ether, washed with 18% NaCl, dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 5.3g (88.7%) of 5, bp 85-88°/0.05 torr.

Anal. Calcd. for $C_{16}H_{30}O_2$ (Mol. Wt. 254)
C, 75.59; H, 11.81
Found C, 75.95; H, 12.05%

ir: ν_{max}(neat)(cm^{-1}): 1640 (double bond), 1135, 1120, 1080, 1030, (-OTHP).

V. Hydroboration and Oxidation of 5[81]: Preparation of 1-tetrahydropyranyloxy undecanal (6)

Under nitrogen, a standardized solution of diborane in THF (0.83M; 34 ml, 0.028 mol) was added, in drops, to ice-cooled and stirred neat olefin 5 (10g, 0.04 mol). The reaction mixture

was left stirred at 0° for 2 hr and then for additional 2 hr at RT, during which period 5 was consumed (tlc). The resulting trialkylborane solution was concentrated **in** vacuo and added, in drops, to a well stirred suspension of pyridinium chlorochromate (26.0g, 0.12 mol) and sodium acetate (1.9g, 0.023 mol) in dry dichloromethane (150 ml). After the initial vigorous reaction had subsided, the stirred mixture was refluxed for 4 hr, cooled to RT, diluted with ether (600 ml), introduced onto a short column of silica gel (d, 2.5 cm, 100g, 100-200 mesh), eluted with ether (200 ml) and solvents evaporated to give 7.612g (71.6%) of 6. The aldehyde 6 was used as such in the following experiment.

ir: ν_{max}(neat)(cm^{-1}): 1730 (aldehyde), 1135, 1120, 1080, 1030, (-OTHP).

VI. Reaction of aldehyde 6 with $Ph_3P{=}CBr_2$[82]: Preparation of 1-tetrahydropyranyloxy 12 gem-dibromo dodec 11-ene (7)

Carbon tetrabromide[83] was prepared conveniently as follows: Bromine (40.0g, 0.25 mol) was added, in drops, to a vigorously stirred and cooled (~0°C) solution of NaOH (30.0g, 0.75 mol) in water (300 ml). After the addition was complete the reaction mixture was left stirred until it attained RT (~2 hr). Freshly distilled bromoform (30.0g, 0.12 mol) was then added, in drops, and the stirring continued for another 5 hr. The precipitated carbon tetrabromide was filtered and dried, yield 34.5g (97.4%), mp 86-89°.

A solution of the aldehyde 6 (7.6g, 0.028 mol) in dry dichloromethane (15 ml) was added, in drops, to the stirred reagent, prepared *in situ* from a mixture of Ph_3P (15.72g, 0.06 mol), CBr_4 (19.68g, 0.06 mol), Zn dust (3.9g, 0.06 mol) and dry CH_2Cl_2 (150 ml) and left stirred for 24 hr. After addition, the reaction mixture was left stirred for additional 2 hr, then diluted with hexane (600 ml), triturated, decanted, the residue treated successively with CH_2Cl_2 (50 ml) and hexane (200 ml), triturated, decanted, and finally the residue treated once again with CH_2Cl_2 (50 ml), hexane (200 ml), triturated and decanted. The combined decanted portions were dried and evaporated to give 9.4g (78.6%) of crude 7 which was used in the following experiment.

ir: ν_{max}(neat)(cm^{-1}): 1620 (double bond), 1135, 1120, 1080, 1030 (OTHP).

VII. Li-Hg debromination of 7: Preparation of the key synthon, 1-tetrahydropyranyloxy dodec 11-yne (8)

Lithium amalgam, (1.5%), was conveniently prepared as follows: clean mercury (100 g) protected by tetralin (30 ml) was heated by an oil bath at 180-190°C. Lithium (1.5g, 0.2 mol), cut into small pieces, was introduced, one by one, pressing each piece down into the hot mercury with a glass rod. After addition, the set up was allowed to attain RT, decanted, the amalgam

repeatedly washed with dry ether, powdered and transferred into a three-necked flask fitted with a mechanical stirrer for the following experiment.

To mechanically stirred 1.5% Li-Hg (100g, 0.2 mol) and dry ether (200 ml) was added, in drops, a solution of 7 (12.0g, 0.028 mol) in dry ether (50 ml). The reaction mixture was left stirred at RT for 20 hr, cautiously treated with water (50 ml), diluted with ether, the organic extract washed with water, brine, dried ($MgSO_4$), evaporated and the residue on distillation gave 3.5g (47%) of pure 8, bp 120-125°/0.2 torr. The yield reflects the fact that the precursors 6 and 7 were used without purification because of their limited stability.

Anal. Calcd. for $C_{17}H_{30}O_2$ (Mol. Wt. 266)

C, 76.69; H, 11.28

Found C, 76.81; H, 10.96%

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.9 (t, 1H, H-C≡C-), 2.25 (m, 2H, -C≡C-CH_2-), 3.2-4.0 (m, 4H, -CH_2-O-THP), 4.58 (s, 1H, -CH_2-O-CH(H)-O-).

VIII. A convenient degradation of n-heptaldehyde (3) to hexanoic acid (10)

a. 1-Acetoxy heptene (9)[84]

A mixture of freshly distilled heptaldehyde (71.0g,

0.622 mol), freshly ignited K_2CO_3 (12.0g, 0.087 mol) and acetic anhydride (140 ml) was refluxed for 1 hr, cooled to RT, washed with warm water, 5% Na_2CO_3, brine, dried ($MgSO_4$) and fractionated to give 60g (76.1%) of 9, bp 88-90°/17 torr and 23.0g of unchanged 3.

ir: ν_{max}(neat)(cm^{-1}): 1760 (acetate), 1675 (double bond).

b. CrO_3 Oxidation of 1-acetoxyheptene (9): Preparation of hexanoic acid (10)

Neat 1-acetoxyheptene (9) (20.0g, 0.13 mol) was added to a stirred solution of the CrO_3-Ac_2O reagent - prepared at 0°, by addition of, in small portions, CrO_3 (38.0g, 0.38 mol) to stirred Ac_2O(400 mol) and then allowed to attain RT - cautiously, in drops, to control the vigorously exothermic reaction. The reaction mixture was left stirred for 3 hr, solvents evaporated in vacuo, the residue admixed with 2N H_2SO_4 (1 l), extracted with benzene, evaporated, the residue triturated with satd. $NaHCO_3$, extracted with ether, the aqueous layer cautiously made acidic (2N HCl), extracted with ether, the organic extract dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 9.87g (66.4%) of hexanoic acid (10), bp 45-46°/0.9 torr.

ir: ν_{max}(neat)(cm^{-1}): 1710 (carboxylic acid), identical to an authentic sample of hexanoic acid.

IX. Transformation of hexanoic acid (10) to hexyl bromide (13)

Fischer esterification of 10 (20g, 0.17 mol) with MeOH-H_2SO_4 (catalyst) gave 22.4g (100%) of methyl hexanoate(11) [bp 150° (ir: ν_{max}(neat)(cm^{-1}): 1742 (ester)] which was transformed to n-hexanol (12), bp 155-156°, in 92% yields, with LAH in ether [ir: ν_{max}(neat)(cm^{-1}): 3360(hydroxyl)]. Reaction with red phosphorus-bromine gave n-hexylbromide (bp 154-156°, 81%) whose ir was identical with that of an authentic sample.

X . Alkylation of 1-tetrahydropyranyloxy dodec 11-yne (8): Preparation of 1-tetrahydropyranyloxy octadec 11-yne(14)

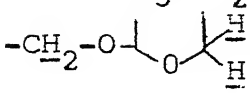
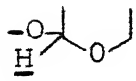
Under nitrogen, n-butyl lithium (1.66g, 0.026 mol) in hexane (11 ml) was added, in drops, to stirred and cooled (< 10°) 8 (3.5g, 0.013 mol) in dry THF (20 ml), followed by a solution of n-hexyl bromide (4.26g, 0.026 mol) in dry HMPT (20 ml), whilst keeping the temperature below 25°. The reaction mixture was left stirred for 0.5 hr, admixed with ice-water, extracted with hexane, the organic layer washed with water, brine, dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 4.32g 94% of 14, bp 140-145°/0.03 torr.

Anal. Calcd. for $C_{23}H_{42}O_2$ (Mol. Wt. 350)

C, 78.85; H, 12.0

Found C, 78.5 ; H, 12.38%

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $\underline{CH_3}-CH_2-$), 2.05 (m, 4H, $-\underline{CH_2}-C\equiv C-\underline{CH_2}-$), 3.15-4.0 (m, 4H, $-\underline{CH_2}-O-$ ), 4.5 (s, 1H, ).

XI. De-protection of 14: Preparation of 1-hydroxy octadec 11-yne (15)

A mixture of 14 (3.0g, 8.6 mmol), ethanol (50 ml) and PPTS (0.224g, 0.86 mmol) was left stirred for ~3 hr at 70°, solvents evaporated in vacuo, the residue admixed with ether (300 ml), washed with brine, dried ($MgSO_4$), solvents evaporated and the residue on distillation gave 2.28g (100%) of 15, bp 103-107°/0.03 torr.

Anal. Calcd. for $C_{18}H_{34}O$ (Mol. Wt. 266)

C, 81.20; H, 12.78

Found C, 81.22; H, 12.30%

ir: ν_{max}(neat)(cm^{-1}): 3330 (hydroxyl)

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $\underline{CH_3}-CH_2-$), 2.1 (m, 4H, $-\underline{CH_2}-C\equiv C-\underline{CH_2}-$), 3.08 (s, 1H, $-CH_2\underline{OH}$), 3.5 (t, 2H, $-\underline{CH_2}-OH$).

XII. Stereoselective hydrogenation of 15: Preparation of 1-hydroxy octadec (Z) 11-ene (16)

A solution of 15 (0.13g, 0.5 mmol) in methanol (5 ml) was partially hydrogenated over 5% Pd on $BaSO_4$ (0.04g), further de-activated with a micro-drop of synthetic quinoline. The hydrogen uptake was carefully monitored and the reaction stopped

soon after the calculated volume was absorbed. The hydrogenation was repeated with several ~ 0.5 mmol batches of 15. The combined crude product on distillation gave a 96% yield of 16, bp 105°/0.03 torr.

Anal. Calcd. for $C_{18}H_{36}O$ (Mol. Wt. 268)

C, 80.6 ; H, 13.43

Found C, 81.0 ; H, 13.15%

ir: ν_{max}(neat)(cm^{-1}): 3330 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2CH=CH-C\underline{H}_2-$), 3.5 (t, 3H, $-C\underline{H}_2-O\underline{H}$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XIII. Oxidation of 16: Preparation of 1-oxo octadec (Z) 11-ene (17), the pheromone of Achroia grisella

Neat 16 (0.48g, 1.8 mmol) was added in one lot to a stirred suspension of pyridinium chlorochromate (PCC) (0.65g, 3.0 mmol) in dry dichloromethane (5 ml). The reaction mixture was left stirred at RT for 2 hr, admixed with dry ether (20 ml), decanted, the residue further extracted with dry ether (3 x 25 ml), the combined extracts passed through a small column (2.5 cm x 10 cm) packed with silica gel and solvents evaporated in vacuo to give 0.46g (96.6%) of 17.

Anal. Calcd. for $C_{18}H_{34}O$ (Mol. Wt. 266)

C, 81.20; H, 12.78

Found C, 81.28; H, 12.76%

ir: ν_{max}(neat)(cm^{-1}): 1730 (aldehyde)

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $\underline{CH_3}$-CH_2-), 1.98 (m, 4H, -$\underline{CH_2}$-CH=CH-$\underline{CH_2}$-), 2.32 (t, 2H, -$\underline{CH_2}$CHO), 5.3 (m, 2H, -$\underline{CH}$=$\underline{CH}$-), 9.65 (t, 1H, -$\underline{CH}$O).

XIV. Direct transformation of 14 to 1-acetoxy octadec 11-yne(18)[85]

A solution of 14 (3.5g, 10 mmol) in AcOH:AcCl::10:1 (11 ml) was left aside overnight, poured onto crushed ice, extracted with hexane, the organic layer washed with 10% $NaHCO_3$, water, brine, dried ($MgSO_4$), evaporated and the residue on distillation gave 2.71g (88%) of 18, bp 106-110°/0.05 torr.

Anal. Calcd. for $C_{20}H_{36}O_2$ (Mol. Wt. 308)

C, 77.92; H, 11.69

Found C, 77.62; H, 11.80%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $\underline{CH_3}$-CH_2-), 1.95 (s, 3H, -OCO$\underline{CH_3}$), 2.05 (m, 4H, -$\underline{CH_2}$-C≡C-$\underline{CH_2}$-), 3.98 (t, 2H, -$\underline{CH_2}$-OCOCH_3).

XV. Stereoselective hydrogenation of 18: Preparation of 1-acetoxy octadec (Z) 11-ene (19), the pheromone of Lycorea ceres ceres

A stirred solution of 18 (0.154g, 0.5 mmol) in methanol (5 ml) was partially hydrogenated as described in Experiment XII. The hydrogen uptake was carefully monitored and the reaction stopped soon after the calculated volume was absorbed. The catalyst was filtered off, solvents evaporated and the residue

chromatographed on a small column of silica gel. Elution with benzene gave 0.15g (96.8%) of 19.

Anal. Calcd. for $C_{20}H_{38}O_2$ (Mol. Wt. 310)

C, 77.42; H, 12.26

Found C, 77.6 ; H, 11.97%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.8 (t, 3H, $C\underline{H}_3-CH_2-$), 1.9 (s, 3H, $-OCOC\underline{H}_3$), 3.93 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

glc: 1.8m x 2mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxy-azobenzene

120° $\xrightarrow{@\ 2^{\circ}/min}$ E:Z::1.7:98.3.

XVI. Alkylation of 1-tetrahydropyranyloxy dodec 11-yne (8): Preparation of 1-tetrahydropyranyloxy hexadec 11-yne(20)

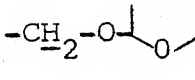
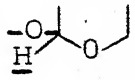
Alkylation of 8 (2.6g, 0.01 mol) with n-butyl bromide (1.6g, 0.012 mol) as described in Experiment X gave 3.01g (95.7%) of 20, bp 137-140°/0.03 torr.

Anal. Calcd. for $C_{21}H_{38}O_2$ (Mol. Wt. 322)

C, 78.26; H, 11.80

Found C, 78.0 ; H, 11.58%

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 2.05 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 3.0-4.0 (m, 4H, $-C\underline{H}_2-O$- ), 4.5 (s, 1H, - ).

XVII. De-protection of 1-tetrahydropyranyloxy hexadec 11-yne (20): Preparation of 1-hydroxy hexadec 11-yne (21)

A solution of 20 (1.2g, 3.7 mmol) and PPTS (0.1g, 0.4 mmol) in ethanol (20 ml) was left stirred at 70° for 3 hr and then processed as described in Experiment XI to give 0.87g (98%) of 21, bp 95°/0.03 torr.

Anal. Calcd. for $C_{16}H_{30}O$ (Mol. Wt. 238)

C, 80.67; H, 12.61

Found C, 81.14; H, 12.4 %

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 2.05 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 2.4 (s, 1H, $-CH_2O\underline{H}$), 3.5 (t, 2H, $-C\underline{H}_2-OH$).

XVIII. Stereoselective hydrogenation of 21: Preparation of 1-hydroxy hexadec (Z) 11-ene (22), the pheromone of Mamestra configurata

A stirred solution of 21 (0.120g, 0.5 mmol) in methanol (5 ml) was partially hydrogenated as described in Experiment XII. Elution with benzene:ethyl acetate::85:15 gave 0.112g (92.6%) of 22.

Anal. Calcd. for $C_{16}H_{32}O$ (Mol. Wt. 240)

C, 80.0 ; H, 13.33

Found C, 80.35; H, 12.88%

ir: ν_{max}(neat)(cm^{-1}): 3320 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 2.8 (s, 1H, $-CH_2-O\underline{H}$), 3.5 (t, 2H, $-C\underline{H}_2-OH$), 5.3 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XIX. Direct transformation of 20 to 1-acetoxy hexadec 11-yne(23)

A solution of 20 (0.65g, 2.0 mmol) in AcOH:AcCl::10:1 (11 ml) was left aside overnight. Work-up as described in Experiment XIV gave 0.47g (83.2%) of 23, bp 90°/0.03 torr.

Anal. Calcd. for $C_{18}H_{32}O_2$ (Mol. Wt. 280)

C, 77.14; H, 11.43

Found C, 76.88; H, 11.2%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 7H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.98 (t, 2H, $-C\underline{H}_2-OCOCH_3$).

XX. Stereoselective hydrogenation of 23: Preparation of 1-acetoxy hexadec (Z) 11-ene (24), the pheromone of Scotogramma trifolii

A stirred solution of 23 (0.140g, 0.5 mmol) in methanol (5 ml) was partially hydrogenated over 5% $Pd/BaSO_4$ as described in Experiment XII. Elution with benzene gave 0.136g (96.5%) of 24.

Anal. Calcd. for $C_{18}H_{34}O_2$ (Mol. Wt. 282)

C, 76.60; H, 12.06

Found C, 76.65; H, 11.78%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $\underline{CH_3}$-CH_2-), 1.95 (m, 7H, -$\underline{CH_2}$-CH=CH-$\underline{CH_2}$-, -OCO$\underline{CH_3}$), 3.95 (t, 2H, -$\underline{CH_2}$OCOCH_3), 5.3 (m, 2H, -$\underline{CH}$=$\underline{CH}$-).

XXI. Alkylation of 1-tetrahydropyranyloxy dodec 11-yne (8): Preparation of 1-tetrahydropyranyloxy tetradec 11-yne(25)

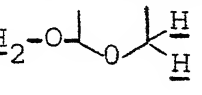
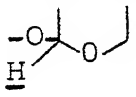
Alkylation of 8 (3.0g, 0.011 mol) with bromoethane (2.59g, 0.024 mol) as described in Experiment X gave 3.1 g (93.4%) of 25, bp 125-130°/0.03 torr.

Anal. Calcd. for $C_{19}H_{34}O_2$ (Mol. Wt. 294)

C, 77.55; H, 11.56

Found C, 77.60; H, 11.20%

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $\underline{CH_3}$-CH_2-), 2.05 (m, 4H, -$\underline{CH_2}$-C≡C-$\underline{CH_2}$-), 3.1-4.0 (m, 4H, -$\underline{CH_2}$-O ), 4.4 (s, 1H, -O ).

XXII. De-protection of 1-tetrahydropyranyloxy tetradec 11-yne(25): Preparation of 1-hydroxy tetradec 11-yne (26)

A solution of 25 (2.0g, 6.8 mmol) and PPTS (0.183g, 0.7 mmol) in ethanol (50 ml) was left stirred at 70° for 3 hr and processed as described in Experiment XI to give 1.3g (91%) of 26, bp 90°/0.03 torr.

Anal. Calcd. for $C_{14}H_{26}O$ (Mol. Wt. 210)

C, 80.0 ; H, 12.38

Found C, 79.61; H, 12.47%

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $C\underline{H}_3-CH_2-$), 2.1 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 2.95 (s, 1H, $-CH_2O\underline{H}$), 3.52 (t, 2H, $-C\underline{H}_2-OH$).

XXIII. Stereoselective hydrogenation of 26: Preparation of 1-hydroxy tetradec (Z) 11-ene (27), the pheromone of Archips rosanus

A stirred solution of 26 (0.21g, 0.001 mol) in methanol (5 ml) was partially hydrogenated as described in Experiment XII. Elution with benzene:ethyl acetate::85:15 gave 0.205g (96.7%) of 27.

Anal. Calcd. for $C_{14}H_{28}O$ (Mol. Wt. 212)

C, 79.24; H, 13.2

Found C, 79.1 ; H, 13.18%

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.5 (t, 3H, $-C\underline{H}_2O\underline{H}$), 5.2 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XXIV. Direct transformation of 25 to 1-acetoxy tetradec 11-yne(28)

A solution of 25 (1.0g, 3.4 mmol) in AcOH:AcCl:10:1 (11 ml) was left aside overnight. Work up as described in Experiment XIV gave 0.78g (91%) of 28, bp 112-115°/0.03 torr.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)

C, 76.19; H, 11.11

Found C, 75.95; H, 10.80%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 1.1 (t, 3H, $C\underline{H}_3-CH_2-$), 1.8 (s, 3H, $-OCOC\underline{H}_3$), 2.1 (m, 4H, $-C\underline{H}_2-C\equiv C-C\underline{H}_2-$), 3.9 (t, 2H, $-C\underline{H}_2OCOCH_3$).

XXV. Stereoselective hydrogenation of 28: Preparation of 1-acetoxy tetradec (Z) 11-ene (29), the pheromone of Choristoneura rosaceana

A stirred solution of 28 (0.252g, 0.001 mol) in methanol (5 ml) was partially hydrogenated over 5% $Pd/BaSO_4$ as described in Experiment XII. Elution with benzene gave 0.248g (97.6%) of 29.

Anal. Calcd. for $C_{16}H_{30}O_2$ (Mol. Wt. 254)

C, 75.59; H, 11.81

Found C, 75.78; H, 11.64%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 2.05 (m, 7H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.95 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.28 (m, 2H, $-C\underline{H}=C\underline{H}-$).

glc: 1.8m x 2mm i.d. 5% 4-(p-methoxycinnamyloxy)-4'-methoxyazobenzene on Gas Chrom Q.

120° $\xrightarrow{@\ 20^{\circ}/min}$ E:Z::5:95

XXVI. Sodium-liquid ammonia reduction of 1-tetrahydropyranyloxy tetradec 11-yne (25): Preparation of 1-tetrahydropyranyloxy tetradec (E) 11-ene (30)

Sodium (1.15g, 0.05 mol) was added, in two lots, to a stirred solution of the acetylene 25 (4.0g, 0.014 mol) in liquid

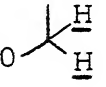
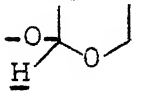
ammonia (50 ml) and dry THF (50 ml), the reaction mixture left stirred until the blue colour was discharged, the ammonia allowed to evaporate, treated with saturated aqueous ammonium chloride (20 ml), poured onto hexane (150 ml), washed with water, brine, dried ($MgSO_4$) and evaporated to give 3.6g (89.3%) of 30.

Anal. Calcd. for $C_{19}H_{36}O_2$ (Mol. Wt. 296)

C, 77.03; H, 12.16

Found C, 76.92; H, 12.31%

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.0-4.0 (m, 4H, $-C\underline{H}_2-O$ ), 4.5 (s, 1H, ), 5.32 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XXVII. De-protection of 1-tetrahydropyranyloxy tetradec (E) 11-ene (30): Preparation of 1-hydroxy tetradec (E) 11-ene(31), the pheromone of Archips argyrospylus

A solution of 30 (1.2g, 4 mmol) and PPTS (0.1g, 0.4 mmol) in ethanol (20 ml) was left stirred at 70° for 3 hr and processed as described in Experiment XI to give 0.77g (89.6%) of 31.

Anal. Calcd. for $C_{14}H_{28}O$ (Mol. Wt. 212)

C, 79.24; H, 13.21

Found C, 79.56; H, 13.28%

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 3.5 (m, 3H, $-C\underline{H}_2-O\underline{H}$), 5.32 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XXVIII. Direct transformation of 30 to 1-acetoxy tetradec (E) 11-ene (32), the pheromone of Platyonota stultana

A solution of 30 (0.6g, 2 mmol) in AcOH:AcCl::10:1 (11 ml) was left aside overnight. Work-up as described in Experiment XIV gave 0.45g (87.6%) of 32.

Anal. Calcd. for $C_{16}H_{30}O_2$ (Mol. Wt. 254)
C, 75.59; H, 11.81
Found C, 75.11; H, 12.07%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 1.95 (m, 7H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.98 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.32 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XXIX. De-protection of 1-tetrahydropyranyloxy dodec 11-yne (8): Preparation of 1-hydroxy dodec 11-yne (33)

A solution of 8 (2.7g, 0.01 mol) and PPTS (0.26g, 0.001 mol) in ethanol (20 ml) was left stirred at 70° for 3 hr and processed as described in Experiment XI. Elution with benzene:ethyl acetate ::90:10 gave 1.80g (97.8%) of 33.

Anal. Calcd. for $C_{12}H_{22}O$ (Mol Wt. 182)
C, 79.12; H, 12.09
Found C, 79.24; H, 11.91%

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl), 3310 ($-C\equiv C-H$), 2120 ($-C\equiv C-$).

nmr: $\delta_{(CCl_4)}$: 1.79 (t, 1H, H-C≡C-), 2.05 (m, 2H, H-C≡C-CH_2-), 2.83 (s, 1H, -CH_2-OH), 3.4 (t, 2H, -CH_2-OH).

XXX. Oxidation of 1-hydroxy dodec 11-yne (33): Preparation of dodec 11-ynoic acid (34)

Jones' reagent [prepared from CrO_3 (1.4g, 0.014 mol), water (2 ml) and conc. H_2SO_4 (0.12 ml, 0.02 mol)] was cooled (~0°) and added, in drops, to a stirred solution of 33 (1.8g, 0.01 mol) in acetone (5 ml), maintaining the temperature below 20°. The reaction mixture was left stirred for 3 hr, diluted with ether, washed with aqueous $NaHSO_3$, water, brine, dried ($MgSO_4$) and evaporated to give 1.69g (87.2%) of 34, bp 76°/0.03 torr.

Anal. Calcd. for $C_{12}H_{20}O_2$ (Mol. Wt. 196)
C, 73.47; H, 10.20
Found C, 73.59; H, 9.94%

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1710 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 1.69 (t, 1H, H-C≡C-), 2.1 (m, 4H, H-C≡C-CH_2-, -CH_2-COOH), 11.2 (s, 1H, -COOH).

XXXI. Alkylation of dodec 11-ynoic acid (34): Preparation of octadec 11-ynoic acid (35)

Under nitrogen, a solution of n-butyl lithium (0.69g, 0.015 mol) in ether (15 ml) was added to a stirred and cooled (~0°C) solution of dodec 11-ynoic acid (34) (1.0g, 0.005 mol)

in HMPT (25 ml) followed by, in drops, neat hexyl bromide (1.6g, 0.01 mol). The reaction mixture was left stirred overnight at RT, poured onto ice water, extracted with ether, the aqueous layer acidified with cold 2N H_2SO_4, extracted with ether, washed with brine, dried ($MgSO_4$), solvents evaporated to give 1.2g (83.9%) of 35, bp 85-87°/0.03 torr.

ir: ν_{max}(neat)(cm^{-1}): 1710 (carboxylic acid).

XXXII. Stereoselective hydrogenation of 35: Preparation of octadec (Z) 11-enoic acid (36, vaccenic acid)

A solution of 35 (0.132g, 0.47 mmol) in methanol (5 ml) was partially hydrogenated over 5% Pd/$BaSO_4$ as described in Experiment XII, and distilled to give 0.124g (93.2%) of 36, bp 105°/0.05 torr.

Anal. Calcd. for $C_{18}H_{34}O_2$ (Mol. Wt. 282)
C, 76.59; H, 12.06
Found C, 76.82; H, 12.38%

ir: ν_{max}(neat)(cm^{-1}): 1710 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 1.82 (t, 3H, $C\underline{H}_3-CH_2-$), 1.9 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 2.2 (t, 2H, $-C\underline{H}_2COOH$), 5.19 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XXXIII. Attempted $-CH=CH_2 \longrightarrow -CH_2-C\equiv C-H$ change with 2: Isolation of methyl dodec 11-ynoate (40) and trideca 1,12 diyne (41)

Methyl undec 10-enoate, (2) (20.0g, 0.1 mol), was processed through sequence, B_2H_6 addition -PCC oxidation, $Ph_3P=CBr_2$ Wittig reaction and Li-Hg treatment as described in Experiments V, VI and VII. The resulting product (7.0g, bp 50-52°/0.03 torr), consisted of two closely moving components (tlc, benzene) and GC on 3% SE-30 column showed that their composition was roughly 1:1. A portion of the crude product was chromatographed on silica gel. Elution with hexane:benzene::80:20 gave the diyne 41:

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-).

nmr: $\delta_{(CDCl_3)}$: 1.68 (t, 2H, H-C≡C-), 2.05 (m, 4H, H-C≡C-CH_2-).

Further elution with hexane:benzene::25:75 gave the yne ester 40

Anal. Calcd. for $C_{13}H_{22}O_2$ (Mol. Wt. 210)

C, 74.29; H, 10.48

Found C, 74.6 ; H, 10.7 %

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 1.95 (t, 1H, H-C≡C-), 2.35 (m, 4H, H-C≡C-CH_2-, -CH_2-$COOCH_3$), 3.72 (s, 3H, -$COOCH_3$).

XXXIV. The preparation of t-butyl undec 10-enoate (42)

In a Paar pressure vessel, isobutylene (10 ml) [prepared from oxalic acid (10.0g, 0.08 mol) and dry t-butanol (20 ml)[86]]

was admixed with a cooled ($\sim -30^{o}$) solution of undec 10-enoic acid (10.0g, 0.054 mol) [prepared from aqueous KOH saponification of methyl undec 10-enoate (2)] and conc. H_2SO_4 (0.5g) in dry dichloromethane (10 ml). The vessel was closed, left stirred at RT for 36 hr, cautiously opened, the contents poured onto water, extracted with ether (3 x 100 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated. The resulting crude product was chromatographed on a short column of silica gel. Elution with benzene gave 8.2g (63%) of 42.

Anal. Calcd. for $C_{15}H_{28}O_2$ (Mol. Wt. 240)

C, 75.0 ; H, 11.67

Found- C, 75.36; H, 11.82%

ir: ν_{max}(neat)(cm^{-1}): 1730 (ester), 1635 (double bond).

nmr: $\delta_{(CCl_4)}$: 1.4 (s, 9H, $-COOC(\underline{CH}_3)_3$), 2.05 (m, 4H, $H_2C=CH-\underline{CH}_2-$, $-\underline{CH}_2-COO^tBu$), 4.85 (m, 2H, $\underline{H}_2C=CH-$), 5.75 (m, 1H, $H_2C=\underline{CH}-$).

XXXV. The transformation of t-butyl undec 10-enoate (42) to t-butyl dodec 11-ynoate (45)

The hydroboration - oxidation of t-butyl undec 10-enoate (42)(8.0g, 0.033 mol) by procedures described in Experiment V, gave smoothly the aldehyde ester 43 (75.2%) which was transformed, in 63% yields, to the dibromide 44 and then to the acetylene 45 (46%) by procedures described in Experiments VI and VII.

43: ir: ν_{max}(neat)(cm^{-1}): 1730 (broad, aldehyde, ester).

44: ir: ν_{max}(neat)(cm^{-1}): 1730 (ester), 1620 (double bond).

45: Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)

C, 76.19; H, 11.11

Found C, 76.63; H, 10.82%

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1730 (ester).

nmr: $\delta_{(CCl_4)}$: 1.4 (s, 9H, $-COOC(\underline{CH}_3)_3$), 1.78 (t, 1H, $\underline{H}$-C≡C-), 2.1 (m, 4H, H-C≡C-$\underline{CH}_2$-, $-\underline{CH}_2COO^tBu$).

XXXVI. Degradation of methyl undec 10-enoate (2) to methyl non 8-enoate (56)

The transformation of methyl undec 10-enoate (2) to methyl dec 9-enoate (49) was carried out by procedures reported from our laboratory (Tetrahedron 36, 1869 (1980)). The observed physical data (ir, nmr) of the compounds involved were in excellent accord with that reported.

a. Addition of PhMgBr to 49: Preparation of the adduct 50

To a well stirred solution of PhMgBr [prepared from Mg (9.6g, 0.4 mol) and bromobenzene (62.8g, 0.4 mol)] in ether (500 ml), was added, in drops, over 1 hr, keeping the temperature below 20°, a solution of methyl dec 9-enoate (49) (36.8g, 0.2 mol) in ether (500 ml). The mixture was refluxed for 2.5 hr, the Grignard complex decomposed with ice cold 2N H_2SO_4, extracted

with ether, washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to yield 60.4g (98%) of the alcohol 50 which was used as such for the following experiment.

ir: ν_{max}(neat)(cm^{-1}): 3460 (hydroxyl), 1632 (double bond), 1590 (phenyl).

b. Dehydration of alcohol 50: Preparation of diene 51

Neat alcohol 50 (60.4g) was held at 200° for 0.5 hr and fractionally distilled to give 47.3g (83.2%) of 51, bp 175°/0.1torr.

Anal. Calcd. for $C_{22}H_{26}$(Mol. Wt. 290)

C, 91.03; H, 8.96

Found C, 90.84; H, 9.16%

ir: ν_{max}(neat)(cm^{-1}): 1640 (double bond), 1600 (phenyl).

nmr: $\delta_{(CCl_4)}$: 2.03 (m, 4H, $-C\underline{H}_2-CH=CH-$), 4.9 (m, 2H, $C\underline{H}_2=CH-$), 5.85 (m, 1H, $CH_2=C\underline{H}-$), 7.12 (m, aromatic).

c. Oxidation of diene 51: Preparation of non 8-enoic acid (52)

To a vigorously stirred solution of 51 (15.6g, 0.054 mol) in glacial acetic acid (250 ml) was added, in drops, over 1.5 hr, a solution of chromium trioxide (14.0g, 0.14 mol) in water (15 ml). After an additional 0.5 hr stirring the reaction mixture was poured onto ice cold 2N H_2SO_4 (0.75 l), extracted with benzene (5 x 100 ml) and evaporated. The residue was triturated with satd. $NaHCO_3$ and extracted with ether (2 x 100 ml). The aqueous layer was carefully acidified with ice cold 2N HCl, extracted

with ether (3 x 100 ml), the organic extracts washed with brine, dried ($MgSO_4$) and evaporated to give 5.26g (62.7%) of 52, bp 75°/0.05 torr.

Anal. Calcd. for $C_9H_{16}O_2$ (Mol. Wt. 156)

C, 69.23; H, 10.25

Found C, 69.66; H, 9.87%

ir: ν_{max}(neat)(cm^{-1}): 1710 (carboxylic acid), 1635 (double bond).

nmr: $\delta_{(CCl_4)}$: 2.0 (m, 2H, CH_2=CH-$C\underline{H}_2$-), 2.3 (t, 2H, -$C\underline{H}_2$COOH), 4.95 (m, 2H, $C\underline{H}_2$=CH-), 5.75 (m, 1H, CH_2=$C\underline{H}$-), 11.7(s,1H,-COO$\underline{H}$).

d. Fischer esterification of non 8-enoic acid (52): Preparation of methyl non 8-enoate (56)

A solution of non 8-enoic acid (52) (5.0g, 0.032 mol) in dry methanol (150 ml) was admixed with conc. H_2SO_4 (0.5 ml) and refluxed for 2 hr. Methanol was distilled off, the residue poured onto ice cold water (500 ml), extracted with ether (3 x 100 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to give 5.1g (93.6%) of 56, bp 58-60°/0.3 torr.

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1640 (double bond).

nmr: $\delta_{(CCl_4)}$: 2.1 (m, 4H, CH_2=CH-$C\underline{H}_2$-, -$C\underline{H}_2$COOMe), 3.5 (s, 3H, -COO$C\underline{H}_3$), 4.85 (m, 2H, $\underline{H}_2$C=CH-), 5.65 (m, 1H, CH_2=$C\underline{H}$-).

XXXVII. Fischer esterification of decane 1,10 dioic acid (53): Preparation of dimethyl decane 1,10 dioate (54)

A solution of sebacic acid (53) (30.0g, 0.15 mol) - prepared by fragmentation of castor oil with hot aqueous alkali[87] - in dry methanol (400 ml) was admixed with conc. H_2SO_4 (5.0 ml) and refluxed for 4 hr. Methanol was distilled off, the residue poured onto ice cold water (300 ml), extracted with ether (3 x 100 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to give 31.0g (90.8%) of 54, bp $102^{\circ}/0.05$ torr.

Anal. Calcd. for $C_{12}H_{22}O_4$ (Mol. Wt. 230)

C, 62.61; H, 9.57

Found C, 62.62; H, 9.48%

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.25 (t, 4H, $-C\underline{H}_2-COOMe$), 3.6 (s, 6H, $-CH_2-COOC\underline{H}_3$).

XXXVIII. Partial saponification of 54: Preparation of methyl decane 1,10 dioic acid monoester (55)

Freshly crystallized barium hydroxide octahydrate (12.8g, 0.04 mol) in methanol (80 ml) was added to a stirred solution of 54 (20.0g, 0.087 mol) in benzene (32 ml). The reaction mixture was left stirred at RT for 20 hr, the separated barium salt of 55 collected, decomposed with 10% HCl (200 ml), extracted with benzene (2 x 100 ml), filtered to remove sebacic acid (2.0g) arising from complete saponification, dried (Na_2SO_4) and evaporated to give

8.89g of 55, bp 146°/0.1 torr. The benzene-methanol filtrate after isolation of the barium salt of 55, on evaporation, gave 6.0g of unchanged 54. Yield of 55 based on recovered 54 and sebacic acid, 80.7%.

Anal. Calcd. for $C_{11}H_{20}O_4$ (Mol. Wt. 216)

C, 61.11; H, 9.26

Found C, 60.92; H, 9.48%

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1690 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 2.25 (m, 4H, $-C\underline{H}_2COOMe$, $-C\underline{H}_2COOH$), 3.6 (s, 3H, $-CH_2COOC\underline{H}_3$), 11.6 (s, 1H, $-CH_2COO\underline{H}$).

XXXIX. Oxidative decarboxylation of 55: Preparation of methyl non 8-enoate (56)

a. Preparation of lead tetracetate[88]

To a mechanically stirred and heated (~ 60°) solution of acetic anhydride (15.5g, 0.152 mol) in glacial acetic acid (46.0g, 0.766 mol) was added, in batches, red lead powder (25.0g, 0.0364 mol) maintaining the temperature below 65°, each batch of red lead being added when the colour due to the preceding portion had disappeared. After the addition was over the reaction mixture was heated at 80° for an additional 0.5 hr, cooled, the crude product filtered and dried *in vacuo*; yield 13.0g (81%). Crystallization from a hot solution of 2% acetic anhydride in glacial acetic acid and treatment with animal charcoal gave the reagent as pure, beautiful, white crystals, mp 189°.

b . Decarboxylative elimination of 55

Under nitrogen, a mixture of 55 (10.8g, 0.05 mol), freshly crystallised lead tetraacetate(33.2g, 0.075 mol), pyridine (3.95g, 0.05 mol), cupric acetate (1.7g, 0.0085 mol) and dry benzene (200 ml) was left stirred for 0.25 hr, heated gradually (CAUTION : CO_2 evolution) to reflux which was continued for 3 hr, cooled to RT, ethylene glycol added ($\sim$20 ml), diluted with water, extracted with benzene (3 x 100 ml), the organic extracts washed several times with dilute HNO_3 ($\sim$0.5N), water, satd. $NaHCO_3$, brine, dried ($MgSO_4$), evaporated and the crude product chromatographed on a short column of silica gel (2 cm x 10 cm). Elution with benzene gave 3.8g (45%) of 56.

Anal. Calcd. for $C_{10}H_{18}O_2$ (Mol. Wt. 170)
C, 70.59; H, 10.59
Found C, 70.23; H, 10.8%

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1640 (double bond).

nmr: $\delta_{(CCl_4)}$: 2.1 (m, 4H, CH_2=CH-$C\underline{H}_2$-, -$C\underline{H}_2$COOMe), 3.5 (s, 3H, -COO$C\underline{H}_3$), 4.85 (m, 2H, $C\underline{H}_2$=CH-), 5.65 (m, 1H, CH_2=$C\underline{H}$-).

XL. Bromination-dehydrobromination of methyl non 8-enoate (56): Preparation of non 8-ynoic acid (57)

To an efficiently stirred and an ice cooled solution of methyl non 8-enoate (56) (1.0g, 0.006 mol) in CCl_4 (10 ml), was added bromine (0.96g, 0.006 mol) in CCl_4 (2 ml). The mixture was allowed to attain RT, solvents evaporated in vacuo and the

resulting dibromide admixed with an aqueous solution of KOH [prepared from 3.6g KOH in 10 ml water], heated for 4 hr at 135-145°, cooled, diluted with water, acidified with cold 6N H_2SO_4, extracted with ether (3 x 50 ml), washed with brine, dried ($MgSO_4$) and evaporated to give 0.8g (88.3%) of 57, bp 102-105°/0.1 torr.

Anal. Calcd. for $C_9H_{14}O_2$ (Mol. Wt. 154)
C, 70.13; H, 9.09
Found C, 69.82; H, 9.48%

ir: ν_{max}(neat)(cm^{-1}): 3300 (-C≡C-H), 2120 (-C≡C-), 1710 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 1.72 (t, 1H, H-C≡C-), 2.1 (m, 4H, H-C≡C-CH_2-, -CH_2COOH), 9.88 (s, 1H, -COOH).

XLI. Modified Hunsdiecker reaction of 55: Preparation of methyl 9-bromo nonanoate (58)

Under nitrogen, stirring and irradiation from a 300W tungsten lamp, a mixture of 55 (9.0g, 0.042 mol), carbon tetrachloride (150 ml) and red mercuric oxide (15.1g, 0.07 mol) was brought to reflux and bromine (9.6g, 0.06 mol) was cautiously introduced over ~ 0.1 hr and irradiation and reflux continued for an additional 3 hr. The reaction mixture was cooled to RT, admixed with satd. $NaHCO_3$ (100 ml), stirred vigorously for 0.25 hr, the two phase mixture filtered through a pad of silica gel, washed several times with chloroform, the combined organic

extracts washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$), evaporated and the residue chromatographed on a short column of silica gel. Elution with benzene gave 7.2g (68.8%) of 58.

Anal. Calcd. for $C_{10}H_{19}O_2Br$ (Mol. Wt. 251)

C, 47.81; H, 7.57

Found C, 47.68; H, 7.1%

ir: ν_{max}(neat)(cm^{-1}): 1735 (ester).

nmr: $\delta_{(CCl_4)}$: 2.25 (t, 2H, $-C\underline{H}_2COOMe$), 3.33 (m, 2H, $-C\underline{H}_2-Br$), 3.6 (s, 3H, $-COOC\underline{H}_3$).

XLII. Dehydrobromination of 58: Attempted preparation of methyl non 8-enoate (56); Isolation of 56 and methyl non 7-enoate (59)

Neat 58 (2.51g, 0.01 mol) was added, in drops, to a stirred 1M solution of potassium t-butoxide (1.7g, 0.015 mol) in dry t-butyl alcohol (15 ml) held at 75°, the reaction mixture cooled to RT, poured onto ice cold water (150 ml), extracted with ether, washed several times with cold water, brine, dried ($MgSO_4$), evaporated and the residue chromatographed on silica gel. Elution with benzene gave 0.5g (29.4%) of the olefinic fraction comprising of a mixture of 59 and 56 (NMR).

XLIII. Fischer esterification of non 8-ynoic acid (57): Preparation of methyl non 8-ynoate (60)

Under stirring, a solution of non 8-ynoic acid (5.0g,

0.032 mol) in dry methanol (250 ml) admixed with conc. H_2SO_4 (0.5 ml) was refluxed for 4 hr, solvents evaporated, the residue cautiously poured onto ice cold water (200 ml), extracted with ether (3 x 100 ml), washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to yield 4.7g (86.2%) of 60, bp 62°/0.03 torr.

Anal. Calcd. for $C_{10}H_{16}O_2$ (Mol. Wt. 168)
C, 71.43; H, 9.52
Found C, 71.12; H, 9.52%

ir: ν_{max}(neat)(cm^{-1}): 3300 (-C≡C-H), 2110 (-C≡C-), 1735 (ester).

nmr: $\delta_{(CCl_4)}$: 1.75 (t, 1H, H-C≡C-), 2.2 (m, 4H, H-C≡C-CH_2-, -CH_2-COOMe), 3.6 (s, 3H, -COOCH_3).

XLIV. Lithium aluminium hydride reduction of methyl non 8-ynoate (60): Preparation of 1-hydroxy non 8-yne (61)

A solution of 60 (2.5g, 0.015 mol) in dry ether (15 ml) was added to a well stirred suspension of LAH (1.0g, 0.026 mol) in dry ether (100 ml) maintained at RT. The mixture was left stirred for 2 hr, excess reagent decomposed by cautious addition of cold water, acidified with ice cold 2N H_2SO_4, extracted with ether, washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to give 2.0g (96%) of 61.

Anal. Calcd. for $C_9H_{16}O$ (Mol. Wt. 140)
C, 77.14; H, 11.43
Found C, 77.10; H, 11.12%

ir: ν_{max}(neat)(cm^{-1}): 3460 (hydroxyl), 3300 (-C≡C-H), 2110 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.72 (t, 1H, H-C≡C-), 2.05 (m, 2H, H-C≡C-CH_2-), 3.52 (t, 3H, -CH_2-OH).

XLV. Preparation of 1-tetrahydropyranyloxy non 8-yne (62)

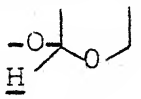
A mixture of 61 (2.0g, 0.014 mol), 5,6-dihydropyran (1.8g, 0.021 mol), PPTS (0.365g, 0.0014 mol) and dry dichloromethane (100 ml) was left stirred at RT for 4 hr, diluted with ether (150 ml), washed with 18% NaCl, dried, evaporated and the residue chromatographed on a short column of silica gel. Elution with benzene gave 2.9g (90.6%) of 62.

Anal. Calcd. for $C_{14}H_{24}O_2$ (Mol. Wt. 224)

C, 75.0 ;H, 10.71

Found C, 74.73;H, 10.48%

ir: ν_{max}(neat)(cm^{-1}): 3300 (-C≡C-H), 2110 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.7 (t, 1H, H-C≡C-), 2.08 (m, 2H, H-C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O- ), 4.5 (s, 1H, ).

XLVI. Alkylation of 1-tetrahydropyranyloxy non 8-yne (62): Preparation of 1-tetrahydropyranyloxy dodec 8-yne (63)

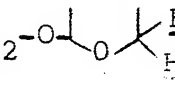
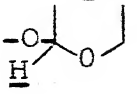
Alkylation of 62 (1.0g, 0.0045 mol) with n-propyl bromide (1.1g, 0.009 mol) as described in Experiment X gave 1.05g (88.2%) of 63.

Anal. Calcd. for $C_{17}H_{30}O_2$ (Mol. Wt. 266)

C, 76.69; H, 11.28

Found C, 76.23 ; H, 11.46%

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.98 (t, 3H, $\underline{CH_3}$-CH_2-), 2.0 (m, 4H, -$\underline{CH_2}$-C≡C-$\underline{CH_2}$-), 3.0-4.0 (m, 4H, -$\underline{CH_2}$-O- ), 4.5 (s, 1H, ).

XLVII. Direct transformation of 63 to 1-acetoxy dodec 8-yne (64)

A solution of 63 (0.7g, 2.6 mmol) in AcOH:AcCl::10:1 (11 ml) was left aside overnight. Work-up as described in Experiment XIV gave 0.49g (83%) of 64.

Anal. Calcd. for $C_{14}H_{24}O_2$ (Mol. Wt. 224)

C, 75.0 ; H, 10.71

Found C, 74.86; H, 10.47%

ir: ν_{max}(neat)(cm^{-1}): 1740 (acetate).

nmr: $\delta_{(CCl_4)}$: 1.95 (s, 3H, -OCO$\underline{CH_3}$), 2.1 (m, 4H, -$\underline{CH_2}$-C≡C-$\underline{CH_2}$-), 4.0 (t, 2H, -$\underline{CH_2}$OCOCH_3).

XLVIII. Stereoselective hydrogenation of 64: Preparation of 1-acetoxy dodec (Z) 8-ene (65), the sex pheromone of Grapholita molesta

A stirred solution of 64 (0.224g, 0.001 mol) in methanol (5 ml) was hydrogenated over 5% Pd/$BaSO_4$ as described in Experiment XII. Elution with benzene gave 0.220g (97%) of 65.

Anal. Calcd. for $C_{14}H_{26}O_2$ (Mol. Wt. 226)

C, 74.34; H, 11.50

Found C, 74.46; H, 11.14%

ir: ν_{max}(neat)(cm^{-1}): 1735 (acetate).

nmr: $\delta_{(CCl_4)}$: 0.9 (t, 3H, $C\underline{H}_3-CH_2-$), 1.92 (m, 7H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$, $-OCOC\underline{H}_3$), 3.9 (t, 2H, $-C\underline{H}_2-OCOCH_3$), 5.28 (m, 2H, $-C\underline{H}=C\underline{H}-$).

XLIX. Sodium borohydride reduction of bromoacetone (66): Preparation of 1-bromo 2-hydroxy propane (67)

Neat bromoacetone (66) (11.0g, 0.08 mol) - freshly prepared by bromination of acetone[89] - was added, in drops, to a stirred and cooled ($\sim 0^{\circ}$) suspension of sodium borohydride (1.5g, 0.04 mol) in dry diglyme (10 ml), the reaction mixture left stirred overnight at RT, excess reagent destroyed by cautious addition of acetic acid, diluted with water, extracted with ether, washed with satd. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated to give 6.5g (58.2%) of 67, bp 146-149°.

ir: ν_{max}(neat)(cm^{-1}): 3360 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 1.3 (d, 3H, $C\underline{H}_3-CH-$), 3.32 (t, 2H, $-C\underline{H}_2Br$), 3.72 (s, 1H, $-CH-O\underline{H}$), 3.9 (m, 1H, $-C\underline{H}(OH)-CH_2-$).

L. Alkylation of non 8-ynoic acid (57): Preparation of 11-hydroxy dodec 8-ynoic acid (68)

A solution of n-butyl lithium (1.28g, 0.02 mol) in ether

(20 ml) was added, in drops, to a stirred and cooled ($\sim 0^{\circ}$) solution of non 8-ynoic acid (57) (1.0g, 0.0065 mol) in HMPT (25 ml), followed by, in drops, neat 67 (1.8g, 0.013 mol) maintaining the temperature at $\sim 0^{\circ}$ and the mixture was left stirred at RT overnight. Work-up as described in Experiment XXXI gave the product (1.0g) which by ir was adjudged to be a $\sim$ 1:1 mixture of 68 and 57. Since their separation was found to be troublesome the crude product was used as such in the next experiment.

ir: ν_{max}(neat)(cm^{-1}): 3400 (hydroxyl), 1710 (carboxylic acid).

LI. Sodium-liquid ammonia reduction of 68: Preparation of 11-hydroxy dodec (E) 8-enoic acid (69)

Sodium (1.15g, 0.05 mol), was added, in two lots, to a stirred solution of 68 (1.0g) in liquid ammonia (50 ml) and dry THF (50 ml), the reaction mixture left stirred until the blue colour was discharged, ammonia allowed to evaporate, acidified with 2N H_2SO_4, poured onto water, extracted with ether, washed with water, brine, dried ($MgSO_4$) and evaporated and the residue containing the desired ω-hydroxy acid 69 was cyclised directly.

LII. Cyclisation[77] of 69: Preparation of 11-hydroxy dodec (E) 8-enoic acid lactone (70)

The crude product from the above experiment (1.0g), 2,2'dipyridyl disulfide (1.65g, 7.5 mol) and triphenylphosphine

(1.97g, 7.5 mmol) were dissolved in dry oxygen-free xylene (100 ml) and left stirred at RT for 5 hr. The resulting solution was then added slowly, over 10 hr, to 500 ml of dry refluxing xylene and the refluxing continued, under nitrogen, for 22 hr, solvents evaporated, the residue extracted with ether, the organic extracts washed with water, brine, dried ($MgSO_4$) and evaporated. The crude product was carefully chromatographed on silica gel. Elution with petroleum ether:ether::95:5 gave 0.05g of 70; tlc:Petroleum ether:Ether::9:1, R_f 0.8, Lit.[76] 0.8.

ir: ν_{max}(neat)(cm^{-1}): 1740 (lactone).

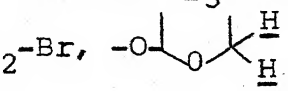
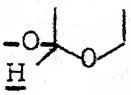
nmr: $\delta_{(CCl_4)}$: 1.4 (d, 3H, $C\underline{H}_3$-CHOCO-), 2.58 (m, 6H, -$C\underline{H}_2$-CH=CH-$C\underline{H}_2$-, -$C\underline{H}_2$-CO-), 5.24 (m, 1H, CH_3-$C\underline{H}$OCO-), 5.5 (m, 2H, -$C\underline{H}$=$C\underline{H}$-).

The above are in agreement with that reported for authentic 70.

LIII. Preparation of 1-bromo 2-tetrahydropyranyloxy propane (71)

A mixture of 67 (14.0g, 0.1 mol), 5,6 dihydropyran (12.7g, 0.15 mol) and PPTS (2.6g, 0.01 mol) in dry dichloromethane (350 ml) was left stirred at RT for 4 hr, solvents evaporated and the residue chromatographed on a column of silica gel. Elution with benzene gave 18.2g (81.6%) of 71.

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.25 (t, 3H, $C\underline{H}_3$-CH(OTHP)-), 3.2-4.1 (m, 5H, CH_3-$C\underline{H}$(OTHP)-$C\underline{H}_2$-Br, ), 4.65 (s, 1H, ).

LIV. Alkylation of 1-tetrahydropyranyloxy undec 10-yne (78) with 71: Preparation of bis 1,13 tetrahydropyranyloxy tetradec 10-yne (72)

Alkylation of 78 (1.26g, 0.005 mol) with 71 (2.23g, 0.01 mol) as described in Experiment X gave 1.5g (76.5%) of 72. ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

LV. Hydroboration-oxidation of methyl undec 10-enoate (2): Preparation of methyl undecane 1,11-dioic acid monoester(73)

A 0.8M solution of BH_3.THF (10 ml, 0.11g, 0.008 mol) was added, in drops, to stirred and cooled ($\sim 0^{\circ}$) methyl undec 10-enoate (2) (5.0g, 0.025 mol). The reaction mixture was left stirred at 0° for 2 hr and then at RT for 2 hr (tlc showed incomplete reaction !), methanol (2 ml) was introduced to destroy excess reagent, if any, and solvents evaporated in vacuo, the resulting trialkylborane dissolved in acetone (15 ml), cooled to 0° and under stirring admixed with, in drops, Jones' reagent [prepared from CrO_3 (5.4g, 0.054 mol), water (7.5 ml) and conc. H_2SO_4 (8.4g, 0.09 mol)], the mixture left stirred for 3 hr at RT, diluted with ether (150 ml), washed with aqueous $NaHSO_3$, water, brine, evaporated, the residue triturated with satd. $NaHCO_3$, extracted with ether (2 x 50 ml), the aqueous layer carefully acidified with ice cold 2N H_2SO_4, extracted with ether (3 x 75 ml), washed with brine, dried ($MgSO_4$) and evaporated to give 1.47g of pure 73 which was used as such for the following experiment.

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1710 (carboxylic acid).

The neutral ether extract was evaporated and chromatographed on a column of silica gel. Elution with benzene gave 2.4g of unchanged 2. Yield based on recovered 2, 49%.

LVI. Oxidative decarboxylation of 73: Preparation of methyl dec 9-enoate (49)

A mixture of 73 (1.0g, 0.004 mol), freshly prepared lead tetraacetate (2.6g, 0.006 mol), cupric acetate (0.14g, 0.007 mol), pyridine (0.316g, 0.004 mol) and dry benzene (20 ml) was left stirred for 0.25 hr and then further processed as in Experiment XXXIX to give 0.29g (36.3%) of 49, bp 60-61°/0.3 torr, whose spectral data was identical to that of an authentic sample.

Anal. Calcd. for $C_{11}H_{20}O_2$ (Mol. Wt. 184)

C, 71.74; H, 10.87

Found C, 71.52; H, 11.19%

ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1655 (double bond).

nmr: $\delta_{(CDCl_3)}$: 3.68 (s, 3H, $-COOCH_3$), 4.9 (m, 2H, $CH_2=CH-$), 5.8 (m, 1H, $CH_2=CH-$).

LVII. Bromination-dehydrobromination of methyl undec 10-enoate (2): Preparation of undec 10-ynoic acid (75)

To a well-stirred and ice cooled solution of methyl undec 10-enoate (2) (40.0g, 0.2 mol) in carbon tetrachloride (150 ml)

was added, in drops, bromine (32.0g, 0.2 mol). The reaction mixture was allowed to attain RT, solvents evaporated, the resulting dibromide (72.2g, 99.8%) suspended in aqueous KOH [prepared from 150g KOH and 90 ml water], efficiently stirred, heated to and held at 150-160° for 8 hr. The tendency for frothing was curbed by the periodical addition of small amounts of sodium lauryl sulfate. Work-up as described in Experiment XL gave 18.0g (50%) of 75, bp 112-115°/0.05 torr.

Anal. Calcd. for $C_{11}H_{18}O_2$ (Mol. Wt. 182)
C, 72.53; H, 9.89
Found C, 72.78; H, 10.12%

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1710 (carboxylic acid).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, H-C≡C-), 2.2 (m 4H, H-C≡C-CH_2-, -CH_2COOH), 11.2 (s, 1H, -COOH).

LVIII. Fischer esterification of undec 10-ynoic acid (75): Preparation of methyl undec 10-ynoate (76)

Under stirring, a solution of undec 10-ynoic acid (18.0g, 0.1 mol) in dry methanol (400 ml) admixed with conc. H_2SO_4 (0.5g) was refluxed for 4 hr. Work-up as described in Experiment XLIII gave 18.5g (95.4%) of methyl undec 10-ynoate (76), bp 70°/0.05 torr.

Anal. Calcd. for $C_{12}H_{20}O_2$ (Mol. Wt. 196)

C, 73.47; H, 10.2

Found C, 73.50; H, 9.93%

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 1.71 (t, 1H, H-C≡C-), 2.15 (m, 4H, H-C≡C-CH_2-, -CH_2COOMe), 3.54 (s, 3H, -COOCH_3).

LIX. Lithium aluminium hydride reduction of methyl undec 10-ynoate (76): Preparation of 1-hydroxy undec 10-yne (77)

A solution of 76 (6.0g, 0.03 mol) in dry ether (20 ml) was added to a well stirred suspension of LAH (2.0g, 0.05 mol) in dry ether (100 ml) maintained at RT. The mixture was left stirred for 2 hr and on work-up as described in Experiment XLIV gave 4.71g (91.6%) of 1-hydroxy undec 10-yne (77).

Anal. Calcd. for $C_{11}H_{20}O$ (Mol. Wt. 168)

C, 78.57; H, 11.9

Found C, 78.99; H, 11.83%

ir: ν_{max}(neat)(cm^{-1}): 3350 (hydroxyl), 3310 (-C≡C-H), 2120 (-C≡C-).

nmr: $\delta_{(CCl_4)}$: 1.8 (t, 1H, H-C≡C-), 2.1 (m, 2H, H-C≡C-CH_2-), 3.55 (t, 3H, -CH_2-OH).

LX. Preparation of 1-tetrahydropyranyloxy undec 10-yne (78)

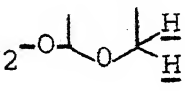
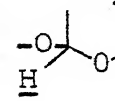
A mixture of alcohol 77 (4.2g, 0.025 mol), 5,6-dihydropyran (3.15g, 0.037 mol), PPTS (0.652g, 0.0025 mol) and dry dichloromethane (150 ml) was left stirred for 4 hr at RT. Work-up as described in Experiment XLV gave 6.272g (99.6%) of 78, bp 95°/0.05 torr.

Anal. Calcd. for $C_{16}H_{28}O_2$ (Mol. Wt. 252)

C, 76.19; H, 11.11

Found C, 76.69; H, 10.89%

ir: ν_{max}(neat)(cm^{-1}): 3310 (-C≡C-H), 2120 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.7 (t, 1H, H-C≡C-), 2.1 (m, 2H, H-C≡C-CH_2-), 3.0-4.0 (m, 4H, -CH_2-O- ), 4.45 (s, 1H, -O- ).

LXI. Hydroxymethylation of 1-tetrahydropyranyloxy undec 10-yne(78): Preparation of 1-tetrahydropyranyloxy 12-hydroxy dodec 10-yne (79)

A solution of n-butyl lithium (2.0g, 0.032 mol) in ether (50 ml) was added, in drops, to a stirred and cooled (0°) solution of 78 (4.0g, 0.016 mol) in dry THF (30 ml). A suspension of paraformaldehyde (1.8g, 0.06 mol) (dried for several days in vacuo over P_2O_5) in THF (20 ml) was then added and the reaction mixture left stirred for an additional 1 hr, poured onto satd. NaCl (150 ml), extracted with ether, dried ($MgSO_4$), evaporated and the

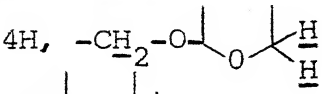
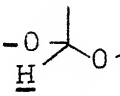
residue fractionated to give 2.85g (63.6%) of 79, bp 157-163°/0.05 torr.

Anal. Calcd. for $C_{17}H_{30}O_3$ (Mol. Wt. 282)

C, 72.34; H, 10.64

Found C, 72.04; H, 10.19%

ir: ν_{max}(neat)(cm^{-1}): 3420 (hydroxyl), 2280, 2220 (-C≡C-), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 2.39 (m, 2H, -C≡C-CH_2-), 2.9 (s, 1H, -CH_2-O$\underline{H}$). 3.3-4.2 (m, 4H, -CH_2-O- ), 4.26 (t, 2H, -CH_2-OH), 4.7 (s, 1H, ).

LXII. Stereoselective hydrogenation of 79: Preparation of 1-tetrahydropyranyloxy 12-hydroxy dodec (Z) 10-ene(80)

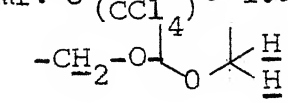
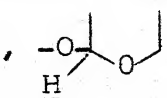
A stirred solution of 79 (0.282g, 0.001 mol) in methanol (5 ml) was partially hydrogenated over 5% Pd/$BaSO_4$ as described in Experiment XII and the crude product chromatographed on silica gel. Elution with benzene:ethyl acetate::90:10 gave 0.273g (96%) of 80. Several 0.001 mol batches of 79 were processed as above, combined and distilled, bp 143-145°/0.07 torr.

Anal. Calcd. for $C_{17}H_{32}O_3$ (Mol. Wt. 284)

C, 71.83; H, 11.27

Found C, 72.12; H, 11.48%

ir: ν_{max}(neat)(cm^{-1}): 3425 (hydroxyl), 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 1.9 (m, 2H, -CH=CH-CH_2-), 2.9-4.0 (m, 7H, -CH_2-O-  , -CH_2-O$\underline{H}$), 4.4 (s, 1H, ).

LXIII. Oxidation of 80: Preparation of 1-tetrahydropyranyloxy 12-oxo dodec (E) 10-ene (81)

Neat alcohol 80 (1.8g, 0.0063 mol) was added, in one lot, to a stirred suspension of PCC (2.15g, 0.01 mol) and sodium acetate (0.4g, 0.005 mol) in dry dichloromethane (20 ml). The reaction mixture was left stirred at RT for 2 hr, diluted with ether (50 ml), filtered through a pad of silica gel, washed repeatedly with ether, the combined filtrate dried ($MgSO_4$) and evaporated to give 1.5g (83.8%) of 81, which was used as such for the following experiment.

ir: ν_{max}(neat)(cm^{-1}): 1730 (aldehyde), 1640 (double bond), 1135, 1120, 1080, 1030 (-OTHP).

LXIV. Preparation of 1-tetrahydropyranyloxy hexadeca (E) 10, (Z) 12-diene (82)

a. Preparation of n-butyltriphenylphosphonium bromide

A solution of n-butyl bromide (15 ml) and triphenylphosphine (5.0g) in dry benzene (5 ml) was refluxed for 4 hr, cooled, the salt collected, washed with dry benzene, dried in vacuo and crystallised from chloroform to give 4.2g of the phosphonium salt, mp 242-243°.

b . Reaction of 81 with n-butyltriphenylphosphonium bromide[90]: Preparation of 1-tetrahydropyranyloxy hexadeca (E)10, (Z) 12-diene (82)

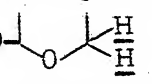
Under nitrogen, to a stirred suspension of freshly prepared n-butyltriphenylphosphonium bromide (4.8g, 0.012 mol) in dry THF (50 ml), was added, in drops, at RT a 0.5M solution of potassium t-butoxide (1.3g, 0.012 mol) in THF (20 ml). The reaction mixture was left stirred for 0.5 hr when an orange yellow precipitate appeared. A solution of 81 (1.5g, 0.0053 mol) in THF (10 ml) was then added, in drops, and stirring continued for an additional 2 hr. The reaction mixture was poured onto satd. NaCl-ether (1:1, 200 ml), the ether layer separated, dried ($MgSO_4$), evaporated and the residue chromatographed over silica gel. Elution with petroleum ether:benzene::75:25 gave 1.1g (64.7%) of 82.

Anal. Calcd. for $C_{21}H_{38}O_2$ (Mol. Wt. 322)

C, 78.26; H, 11.80

Found C, 78.41; H, 12.27%

ir: ν_{max}(neat)(cm^{-1}): 1135, 1120, 1080, 1030 (-OTHP).

nmr: $\delta_{(CCl_4)}$: 0.88 (t, 3H, CH_3-CH_2-), 2.0 (m, 4H, -CH_2(CH=CH)$_2$$CH_2$-), 3.0-4.0 (m, 4H, -$CH_2$-O- ), 4.4 (s, 1H, ), 4.95-6.3 (m, 4H, -CH=CH-CH=CH-).

LXV. De-protection of 82: Preparation of 1-hydroxy hexadeca (E)10, (Z)12-diene (83, bombykol), the insect sex pheromone of Bombyx mori

A mixture of 82 (0.9g, 0.0028 mol), PPTS (0.078g, 0.0003 mol) and ethanol (10 ml) was left stirred at 70° for 4 hr, solvents evaporated in vacuo and the residue chromatographed on silica gel. Elution with benzene: ethyl acetate::90:10 gave 0.65g (97.7%) of 83.

Anal. Calcd. for $C_{16}H_{30}O$ (Mol. Wt. 238)

C, 80.67; H, 12.60

Found C, 80.23; H, 12.82%

ir: ν_{max}(neat)(cm^{-1}): 3340 (hydroxyl).

nmr: $\delta_{(CCl_4)}$: 0.95 (t, 3H, $C\underline{H}_3-CH_2-$), 2.0 (m, 4H, $-C\underline{H}_2-CH=CH-C\underline{H}_2-$), 2.88 (s, 1H, $-CH_2-O\underline{H}$), 3.62 (t, 2H, $-C\underline{H}_2OH$), 5.35 (bt, 1H, $-CH_2-C\underline{H}=CH-CH=CH-$), 5.62 (dt, 1H, $-CH_2-CH=CH-CH=C\underline{H}-$), 5.95(dd, 1H, $-CH_2-CH=C\underline{H}-CH=CH-$), 6.3 (dd,1H, $-CH_2-CH=CH-C\underline{H}=CH-$).

glc: 1.8m x 2mm i.d. 5% 4-(p-methoxycinnanyloxy)-4'-methoxyazobenzene on Gas chrom Q

120° $\xrightarrow{@\ 2°/min}$ 89.3% EZ, 1.6% ZZ, 9.2% EE.

LXVI. Hydroxymethylation of methyl undec 10-ynoate (76): Preparation of 12-hydroxy methyl dodec 10-ynoate (84)

a. Preparation of cuprous oxide[91]

A 20% hydrazine hydrate solution (3-5 ml) was mixed with a

solution of copper II acetate (10.0g) in water (50 ml). After the cessation of nitrogen evolution, the yellowish orange cuprous oxide separated gradually over 1-2 hr. The mixture was filtered, the oxide washed repeatedly with water, alcohol and ether and dried *in vacuo*.

b . Preparation of 12-hydroxy methyl dodec 10-ynoate (84)

A mixture of methyl undec 10-ynoate (76) (8.0g, 0.04 mol), aqueous formaldehyde (30%, 20 ml), freshly prepared cuprous oxide (4.0g, 0.03 mol) and dioxan (35 ml) was refluxed under nitrogen for 48 hr, cooled to RT, acidified with HCl (2N), extracted with ether, (3 x 100 ml), washed ether extracts with HCl (3N), dried ($MgSO_4$) and evaporated. Fractionation of the residue gave 2.4g (26.3%) of 84, bp 133-137°/0.4 torr.

Anal. Calcd. for $C_{13}H_{22}O_3$ (Mol. Wt. 226)

C, 69.01; H, 9.73

Found C, 68.82; H, 9.98%

ir: ν_{max}(neat)(cm^{-1}): 3460 (hydroxyl), 2280, 2220 (-C≡C-), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.21 (m, 4H, -C≡C-C$\underline{H}_2$-, -C$\underline{H}_2$COOMe), 3.22 (s, 1H, -$CH_2O\underline{H}$), 3.59 (s, 3H, -COOC$\underline{H}_3$), 4.08 (t, 2H, -C$\underline{H}_2$-OH).

LXVII. Stereoselective hydrogenation of 84: Preparation of 12-hydroxy methyl dodec (Z) 10-enoate (85)

A stirred solution of 84 (0.226g, 0.001 mol) in methanol (5 ml) was partially hydrogenated over 5% $Pd/BaSO_4$ as described in Experiment XII. Several 0.001 mol batches were processed in this way, combined and distilled to obtain a 90% yield of 85, bp 92-96°/0.03 torr.

Anal. Calcd. for $C_{13}H_{24}O_3$ (Mol. Wt. 228)
C, 68.42; H, 10.53

Found C, 68.36; H, 10.24%

ir: ν_{max}(neat)(cm^{-1}): 3400 (hydroxyl), 1740 (ester).

nmr: $\delta_{(CCl_4)}$: 2.2 (m, 4H, $-CH_2COOMe$, $-CH=CH-CH_2-$), 3.25 (s, 1H, $-CH_2-OH$), 3.6 (s, 3H, $-COOCH_3$), 4.03 (t, 2H, $-CH_2-OH$), 5.45 (m, 2H, $-CH=CH-$).

LXVIII. Oxidation of 85: Preparation of methyl 12-oxo dodec (E) 10-enoate (86, traumatin)

Neat alcohol 85 (1.0g, 4.4 mol) was added, in one lot, to a suspension of PCC (1.3g, 6.0 mmol) in dry dichloromethane (5 ml). The reaction mixture was stirred at RT for 2 hr and worked up as described in Experiment LXIII to give 0.67g (68%) of 86; Semicarbazone mp 130-132°.

86: ir: ν_{max}(neat)(cm^{-1}): 1740 (ester), 1720 (aldehyde)

Semicarbazone:

Anal. Calcd. for $C_{14}H_{25}N_3O_3$ (Mol. Wt. 283)

C, 59.36; H, 8.83

Found C, 59.55; H, 8.55%

ir: ν_{max}(KBr): 3470 (-NH), 1740 (ester), 1690 (amide), 1660 (double bond).

nmr: $\delta_{(CCl_4)}$: 2.25 (m, 4H, -C<u>H</u>$_2$-CH=CH-, -C<u>H</u>$_2$COOMe), 3.68 (s, 3H, -COOC<u>H</u>$_3$), 5.62 (br, 2H, -C<u>H</u>=C<u>H</u>-), 6.10 (br, 2H, -CONH$_2$), 7.40 (br, 1H, -N<u>H</u>), 9.65 (br, 1H, -C<u>H</u>=N-).

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VITAE

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